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## STAPHYLOCOCCUS ANTITOXIC SERUM IN THE TREATMENT OF ACUTE STAPHYLOCOCCAL INFECTIONS AND TOXÆMIAS

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### II. WHEN NO STAPHYLOCOCCÆMIA IS DEMONSTRABLE.

A PUBLICATION in the last number of this *Journal*\* put forward arguments providing a rational basis for the use of antitoxic horse serum in the treatment of acute staphylococcal infections and toxæmias in human beings. In the same communication were outlined the results obtained by means of such a serum, prepared by the Connaught Laboratories, in a series of 104 patients. The two supplementary papers supply case histories illustrative of the use of staphylococcus antitoxin in each group of the classification of cases set forth in our former paper. This present report contains representative examples of the treatment with specific antitoxin of acute staphylococcal infections unaccompanied by demonstrable blood stream invasion. In the next report, instances will be given of the antitoxin treatment of infections in which there was the complicating factor of staphylococæmia.

Of the forty patients who may be classed in the former of the two categories, only 4 died, although it seems certain that in the absence of antitoxin therapy many more fatalities would have occurred. The 4 patients who succumbed gave definite indications during the early course of their illness of having been benefited by the administration of antitoxin.

#### ACUTE CARBUNCLE

Of 10 patients with acute carbuncle, 2 were females aged 25 and 45, and 8 were males aged 17, 35, 37, 38, 42, 45, 67 and 68 years respectively. The site of infection was the back of the

neck in 7 cases, in the remaining 3 the buttock, shoulder and upper lip, respectively were involved.

In 3 cases, a deep carbuncle, with tissue destruction of the whole back of the neck, showing no sign of commencing limitation, had been present for several days prior to administration of serum. There was fever to 102°, extreme local pain, and the patients were, clinically, gravely ill. One patient had developed albuminuria, and another glycosuria, since the onset of the infection. Drastic operative procedures were being considered. An average of 60 c.c. of staphylococcus antitoxic serum was given intramuscularly, 30 c.c. into each thigh, either at one time or at a few hours' interval. One patient had chills and a slight febrile reaction within 24 hours of the serum administration; the other patients showed no reaction. Within 2 or 3 days, the temperature had become normal, the spread of the infection was arrested, the pain and swelling had diminished, and an increased discharge of pus was apparent. Two patients showed complete healing in six weeks, and one patient in two months, from the date of giving the serum, without skin grafting or surgical interference of any kind.

Of the other 7 cases, 2 had a carbuncle of the neck, and one had a carbuncle of the back, of lesser magnitude than the above, but accompanied by fever and evidence of general toxæmia. Another had a carbuncle of the buttock with fever, vomiting and an acute inguinal lymphadenitis. Each of these patients received 60 c.c. antitoxin intramuscularly, with the result

\* *Canad. M. Ass. J.*, 1934, 30: 601.

that within 24 to 48 hours extensive and painful induration had softened and was no longer tender, tenacious sloughs had loosened and discharged, and healing had begun, without surgical interference of any kind. One patient, a woman admitted to hospital with a carbuncle of the neck, appeared also to be developing a carbuncle on the nose, but all inflammation rapidly subsided there after the injection of antitoxin. The same rapid and complete resolution without any discharge of pus, occurred in 3 other cases of threatened carbuncle, 2 of the neck and 1 of the upper lip, following intramuscular injection of 30 c.c. and 60 c.c. antitoxin, respectively.

The remaining patient, a middle-aged man subject to boils for many years, had received the second dose of a course of injections of an auto-genous staphylococcus vaccine just prior to the rapid development of a painful lump about the size of a pullet's egg on the back of his neck. His whole scalp was tense with inflammatory œdema, and he felt acutely ill. The local swelling and the widespread œdema completely subsided overnight after administration of 60 c.c. antitoxin intramuscularly. A further 60 c.c. were however given on the second day, as considerable constitutional disturbance was still present. A rapid recovery then ensued. This patient had a rigour about 2 hours after each dose of serum, and a rather troublesome urticaria about one week later. None of the other patients in this group suffered any notable serum reaction.

#### GENERALIZED CARBUNCULOSIS

The following account of a case of generalized carbunculosis illustrates several points of interest. A woman of 65 years, a moderately severe diabetic of some 5 years' standing, was admitted to the Royal Victoria Hospital, Montreal, with cystitis, bilateral hydronephrosis and nephroptosis. A catheter specimen of urine grew *Staphylococcus aureus*. Soon after admission a uterine cervical polypus was removed. Following this operation signs of pneumonia appeared in the left upper lobe, which cleared up in 3 days. Six days later multiple boils appeared on the buttocks and hips, rapidly assuming the characteristics of spreading carbuncles. Fresh lesions continued to appear during the next 8 days, and the patient was dangerously ill from the increasing sepsis. The white blood count was 13,600, temperature 102°,

pulse 80, respirations 24, blood pressure 112/52. Following the recommendations of Professor Murray, after desensitization had been attempted, 60 c.c. of staphylococcus antitoxin were given intravenously, diluted in physiological saline, over a period of 4½ hours. A severe rigour occurred about 1 hour after the serum injection commenced, and lasted for 20 minutes. At this time the temperature was 98°, pulse 100, respirations 40, blood pressure 140/62, and the white blood count 10,150. The temperature then rose rapidly, and 2 hours later was 106° by rectum, pulse 136, respirations 40, while the blood pressure had fallen to 78/20. The temperature fell sharply from this high point after 3 hours, but the blood pressure was still at a very low level 7 hours after serum administration had ceased, and reached a minimum of 62/38 before gradually improving. Six hours after the serum had all been given, the white blood cells were 30,000, the carbuncles showed definite evidence of localization, became soft, and sloughed their necrotic centres. Twelve days later, active immunization with staphylococcus toxoid was commenced, and the patient was discharged free of carbuncles one month after their first appearance. The patient's diabetic condition remained under control throughout her illness. Dr. E. H. Mason, whose patient she was, and to whom I am indebted for the details included in his report, wrote as his opinion that "the antitoxin had a very definite therapeutic effect for the good, and if the patient had not received the antitoxin her prognosis would have been very doubtful indeed."

The staphylococcal infection of the urinary tract and the transitory pneumonia which preceded the outbreak of carbuncles in this patient seem of special significance. Similar observations have been made in other cases, and these will be noted later. In the light of subsequent experience it appears probable that the same end-result might have been attained in this case if the serum had been given by the intramuscular route, and the grave reaction which followed its intravenous administration could thus have been avoided. A reaction of the type described has almost invariably followed intravenous administration of our staphylococcus antitoxin.

#### GENERALIZED FURUNCULOSIS

Of the first clinical group of Table I in our foregoing paper, there remain 3 cases of gen-

eralized furunculosis. Two of these were infants about 3 months old, with lesions not sufficiently extensive for their disappearance to be attributed with certainty to the serum therapy.

The third case, a boy of 5 years, had been admitted one month previously to St. Michael's Hospital, Toronto, under the care of Dr. E. A. Broughton, with signs of broncho-pneumonia of both lungs. The patient had become very weak and emaciated, but his lungs appeared to be slowly clearing, when one day a high fever returned, and the throat was found acutely inflamed. Two days later an outbreak of furuncles appeared on the neck, buttocks, upper and lower extremities, and eyelids. Some of these furuncles discharged staphylococcal pus and healed, but the majority developed slowly, so that by the end of a week numerous indolent furuncles of various sizes were present all over the body. The patient appeared acutely ill. Thirty c.c. of staphylococcus antitoxin were given intramuscularly. A severe serum reaction occurred 11½ hours later, and the boy's condition was poor for 24 hours following the serum administration. But next day his general condition was much improved; no fresh furuncles appeared, and existing lesions seemed to be clearing up. Two days later, 6 large boils were opened, and each found to contain about 3 drachms of creamy pus. Thenceforward, rapid and steady progress was made, so that two weeks later there was no evidence of furunculosis, while a few râles in one lung was the only remaining sign of the chest infection.

#### ACUTE GENERALIZED BULLOUS DERMATITIS

A brief account will be given of two cases in this group.

A healthy baby of normal weight, was delivered by Cæsarean section from a mother who had mastitis and phlebitis. The infant on the fourth day developed blebs and pustules on the perineum, whence a bullous rash spread over the whole body, with large confluent blebs on neck, vulva, and perineum. Abundant staphylococci were present in the fluid from the primary vesicles. Numerous antiseptic local applications failed to arrest spread of the lesions. By the eleventh day, the infant was critically ill, vomited frequently, the whole body was cyanosed, respirations and pulse were extremely rapid, temperature was 104°, and 17 ounces in weight had been lost. A fatal issue was antici-

pated by the attending physicians. At this juncture, 10 c.c. staphylococcus antitoxin were given intramuscularly, and repeated at 12-hour intervals to a total of 30 c.c. An abrupt rise in temperature followed the first two injections of serum. Twelve hours after the first injection the baby seemed better, and within 24 hours the cyanosis had gone, 2½ ounces were gained, all lesions appeared to be healing, and no new ones developed. The infant left hospital 10 days later, with all lesions healed, normal temperature, and gaining weight well. For this report I am indebted to Dr. J. H. Davidson of Niagara Falls, and to Dr. Roy Simpson of Toronto.

A girl aged 3½ years was admitted to the Hospital for Sick Children, Toronto, under the care of Dr. Alan Brown, with a generalized vesicular rash and confluent dark red patches of inflammatory necrosis around the neck and back, and large bullæ about 5 by 2 inches on the chest and arms. The buccal mucous membrane was ulcerated, and the fauces congested. The child was very drowsy, with twitching extremities, and temperature to 104.6°. The condition had begun 5 days earlier with blood-shot eyes, fever, and a few small vesicles under the chin and on the shoulders. *Staphylococcus aureus* and an occasional hæmolytic streptococcus could be grown from the vesicular fluid. Blood culture proved sterile; white blood cells were 10,200. On the third day after admission to hospital, 40 c.c. staphylococcus antitoxin were given intramuscularly, and 60 c.c. on the following day. Very little serum reaction was noted, and the toxic symptoms rapidly subsided. The fever abated within 2 days, and the lesions began to epithelialize. Ten days after receiving the serum, the patient left hospital with all the crusts off and no open lesions.

#### OTHER INFECTIONS OF SKIN AND SUBCUTANEOUS TISSUES BY STAPHYLOCOCCUS

The type of case, the general mode of antitoxin treatment, and the uniformly favourable results obtained in this group, have been already alluded to in the previous paper. A brief case history will now be given of 2 of the patients for whom the prognosis was considered by the various clinicians associated with them to be particularly grave.

A young hospital nurse had an acute lymphangitis of the arm from running a sliver into



her finger a few days earlier. When seen there was fever around  $104^{\circ}$ , the white blood cells were no more than 8,000, there had been vomiting, alternating restlessness and drowsiness, and occasional delirium. The patient received 120 c.c. of antitoxin intravenously over a two-hour period, and 80 c.c. intramuscularly, within the next 48 hours. Two hours after the commencement of the intravenous serum she had a violent rigor, during which the temperature rose to  $107^{\circ}$ . Next morning the temperature was  $99.6^{\circ}$ , but 36 hours later rose again, ranging then for several days from  $98$  to  $103^{\circ}$ ; and for two weeks at least the patient's condition remained quite critical. During this time, an axillary abscess was opened, and the patient exhibited many of the signs and symptoms characteristic of a staphylococcal blood stream infection, including high fever and pulse rate, migratory pains, central nervous system and gastrointestinal disturbances, transitory jaundice, and finally broncho-pneumonia. Blood culture was, however, sterile, except on one occasion, when it yielded a *Staphylococcus albus* of quite different appearance from the aureus strains grown from the finger and axillary abscess pus. This was considered a contaminant. One month after onset of the infection, the patient had completely recovered.

This patient was the only one of this group to receive the serum intravenously. Others were given intramuscularly total amounts of from 60 c.c. to 240 c.c.

A male aged 40 years was admitted to Toronto General Hospital under the care of Drs. Fletcher McPhedran and Roy Thomas, with a history of having punctured his left index finger with glass wool 7 days previously near the site of a small pustule. Shortly after this, the finger showed signs of spread of the local infection, and 2 or 3 days later the patient felt generally ill, with fever, marked abdominal pain and flatulence. These symptoms increased up to the time of admission to hospital, where an incision was made into the infected finger, and the inter-lumbrical space explored. The dorsum of the hand was also incised. Very little frank pus was noted, although the exposed tissues appeared in parts on the verge of necrosis. A swab from these tissues grew a pure culture of *Staphylococcus aureus*. Following the operation, the patient's condition was unimproved, and when seen 48 hours later he looked and felt very toxic,

and had marked abdominal distension with painful flatulence. The temperature was  $102.4^{\circ}$ , pulse 100; there was an acute inflammatory swelling over the dorsum of the left wrist joint, whose movements were exquisitely painful, and also a tender swelling on the buttock. Blood culture at this time gave no growth. The anti-hæmolytic power of his blood serum against staphylococcus toxin was remarkably low. Sixty c.c. staphylococcus antitoxin were given intramuscularly, without resulting serum reaction. Next day the patient had several attacks of tachycardia, during which the heart rate rose as high as 160. Digitalis appeared effectively to control these attacks, but for 2 days the pulse rate was unduly high in proportion to the temperature, a characteristic feature of staphylococcal toxæmia. A further 60 c.c. of antitoxin were given on each of these 2 days. On the following day the patient felt much more comfortable; the temperature was down to  $100^{\circ}$ , and the inflammatory foci of wrist and buttock had almost resolved. But although a blood specimen taken next day showed an eight-fold increase over the initial amount of circulating staphylococcus antitoxin, the titre was still very little higher than that found for the average normal person who has had no recent staphylococcal infection. A final 60 c.c. of antitoxin were therefore given intramuscularly, making a total dosage of 240 c.c. That same evening the patient enjoyed his food for the first time since the onset of the infection. Next day his temperature and pulse rate reached normal limits and the anti-hæmolytic power of his serum against staphylococcus toxin showed a further four-fold increase. Convalescence was uneventful, the patient leaving hospital quite well 12 days after receiving the last dose of serum. Active immunization with staphylococcus toxoid was shortly afterwards begun to guard against recurrences of infection.

#### ACUTE SEPTIC ARTHRITIS

This was a fatal case of staphylococcal toxæmia arising from infection of the right knee joint in a male aged 39, following removal of the internal semilunar cartilage. At the time the serum was given, two weeks after operation, the patient's condition was very poor indeed; temperature was  $102^{\circ}$  by axilla, pulse 124 and weak, respirations 40. He was irrational, had precordial pain, and bowel movements were in-

voluntary. Over a period of 48 hours, 120 c.c. antitoxin were given intramuscularly in 30 c.c. doses. The pulse rate and temperature fell slightly following this treatment, and the discharge of bloody, fœtid pus became very profuse. The patient remained very weak, however, progressive anæmia and anorexia being apparent throughout the succeeding 7 days. Two blood transfusions seemed only to aggravate these symptoms, and death took place 24 days after operation.

#### STAPHYLOCOCCAL EMPYEMA

A girl infant 12 months was admitted to the Hospital for Sick Children, Toronto, under the care of Dr. Alan Brown, with signs of broncho-pneumonia. An empyema developed, from which aspirated fluid grew *Staphylococcus aureus*. Fifteen c.c. of antitoxin were given intramuscularly in 3 doses of 5 c.c. each, at 4-hourly intervals. Next day intercostal drainage was performed, but as the temperature and pulse rate remained high, an additional 15 c.c. were given intramuscularly. The following day the patient seemed much better and made an unexpectedly rapid recovery.

The second patient, a man aged 46, had pneumothorax induced over 7 years previously for pulmonary tuberculosis, of which disease there were no longer any active signs. Regular refills had been made, and shortly after the last one he developed a pyopneumothorax which proved to be due to *Staphylococcus aureus*. One week later he was admitted to St. Michael's Hospital, Toronto, appearing very toxic and cyanosed, with marked loss in weight, and a daily temperature range of from 98 to 103°. Antitoxin was administered intramuscularly on 3 successive days in doses of 30 c.c., 30 c.c., and 60 c.c., respectively. By the day following the last dose of antitoxin, the patient's condition had markedly improved, and next day it was possible to undertake drainage of the cavity without apprehension. The patient made rapid progress, and a few weeks later a partial thoracoplasty for obliteration of the cavity was done. For the notes of this case, as also of the case which follows, I am indebted to Drs. J. H. Elliott and W. G. Carseadden.

The third patient, a student aged 21, was admitted to hospital with symptoms which eventually proved to be due to acute pleurisy. A small ulcer on his chest formed the probable

primary focus for the acute staphylococcal empyema which soon developed. When seen 12 days after admission, the patient was acutely ill, cyanosed, delirious, with abdominal distension, and a daily temperature range of from 99.2 to 104°. About 250 c.c. turbid fluid had been aspirated from the left chest on the 2 preceding days. *Staphylococcus antitoxin* was given intramuscularly to a total amount of 180 c.c. during the next 3 days, following which the patient appeared much improved, so thoracotomy was then performed. The prognosis had formerly been considered very grave by several clinicians who saw him, but was now thought to be fairly good. However, signs slowly developed which, 15 days after the last dose of serum, were definitely attributed to meningitis. This was thought from its insidious onset to be probably tuberculous, but the cerebrospinal fluid, which had proved sterile on several previous occasions, next day grew *Staphylococcus aureus*. An extra-dural abscess of the lumbar region was located, which probably represented an extension of infection along the epidural space from the thoracotomy wound, and laminectomy was performed with a view to its drainage. The patient had a complete paraplegia and died six weeks after meningitis was definitely diagnosed. The long survival in the face of a hopeless type of infection surprised all associated with this case, and was probably due to his high titre of circulating staphylococcus antitoxin, which dated from the time of absorption of the antitoxic serum.

#### STAPHYLOCOCCAL MENINGITIS AND/OR BRAIN ABSCESS

A girl of 3½ years was admitted to the Hospital for Sick Children, Toronto, acutely ill with signs and symptoms of pyelitis and meningitis. She had fallen downstairs 2 days previously, and there was a large hæmatoma over the right frontal region. Pus and considerable albumin were present in the urine, but blood culture proved sterile, and at this time the cerebrospinal fluid gave no growth, and showed only one to two cells per c.mm. Twelve days after admission, *Staphylococcus aureus* was grown from the cerebrospinal fluid, which was cloudy and found to contain 2,000 polymorph cells per c.mm. The temperature in the meantime had ranged from 100 to 104°, and the pulse rate from 120 to 140. Three days later, 18 c.c.

staphylococcus bacteriophage were given intravenously. The following day a further 18 c.c. were given intravenously, and next day 18 c.c. intrathecally. Although *in vitro* this bacteriophage lysed the particular strain of *Staphylococcus aureus* isolated from the child's cerebrospinal fluid *in vivo*, as was rather to be anticipated from its demonstrable inactivation by blood and tissue fluids, it proved ineffectual. During these 3 days the temperature ranged from 102 to 104°, the pulse from 130 to 150, the cerebrospinal fluid remained just as cloudy and still grew staphylococcus aureus. Next day 21 c.c. staphylococcus antitoxin were given intrathecally, and on the succeeding 2 days, 22 c.c. and 25 c.c. were given by the same route. On the day following the first dose of serum the temperature assumed a lower level, ranging from 100 to 102° for 3 days, after which 100° became the maximum level until the child was transferred to convalescent hospital 3 weeks later. At this time some stiffness of the legs was still present, but no other signs of residual meningeal irritation, a mild degree of bronchitis, and an unduly high pulse rate, averaging 120. Three months later she was discharged quite well.

The following case is recorded in some detail because the unanimous opinion of those who came into contact with it was that recovery would not have taken place without antitoxin therapy; and also because it illustrates well the value of promptitude in the diagnosis of staphylococcal infection.

A girl aged 24 was admitted to the Royal Victoria Hospital, Montreal, under the care of Dr. W. Penfield, with 8 years' history of grand mal attacks, one or two every 3 weeks to 3 months. Two years before their onset a right frontal abscess of unknown etiology had been successfully drained at the Mayo Clinic. Encephalography suggested a contractile scar in the right frontal region, and this scar was removed on October 7, 1933, by Dr. Penfield. For the first 6 days following operation, the temperature ranged from 100 to 130°, but next day (October 13th) it fell to 98.8°. All sutures were removed and the suture line looked well. The same evening, temperature rose to 103.8°, and on October 15th a cerebrospinal fluid leak developed in the upper edge of the operative wound. The white blood count of the fluid was 1,300 polymorphs per c.mm.; direct smears

showed Gram-positive cocci, both intracellular and extracellular. The fluid was cultured at once and *Staphylococcus aureus* was reported the next day to have grown. As the patient was sensitive to horse serum, desensitization was carried out on October 15th, and on the same day 80 c.c. of staphylococcus antitoxin, manufactured elsewhere, were given intramuscularly, and 40 c.c. intravenously, upon the advice of Professor Murray. Next day, a further 40 c.c. of this antitoxin were given intramuscularly. Cisternal puncture at this time yielded fluid with white blood cells, 11,000, while staphylococci, some of them intracellular, could be seen in the direct smear. Between October 17th and 19th, 30 c.c. of antitoxin were given intracisternally, and 80 c.c. intramuscularly. Cisternal and ventricular fluid continued to grow staphylococcus aureus. Beginning October 20th, for 3 successive days, staphylococcus antitoxin prepared by the Connaught Laboratories was given in daily dosage of 40 c.c. intramuscularly and 10 c.c. intracisternally. No further serum was then given intracisternally, for on October 23rd the cisternal fluid proved sterile, and remained so thereafter. However, discharge from the drainage tube in the wound continued to grow *Staphylococcus aureus*, and serum was therefore still given intramuscularly, 40 c.c. on October 23rd, 60 c.c. on the 24th, about 10 c.c. daily thereafter until November 2nd, and then an occasional dose of 5 c.c. or 10 c.c. up to November 19th. In all, 670 c.c. of antitoxin were given, of which the last 400 c.c. were the Connaught Laboratories' preparation. Until October 28th, the patient's temperature underwent wide daily fluctuations, the extreme limits throughout this period being 99° and 104.6°. On that day, drainage of cerebrospinal fluid from the wound ceased, the temperature assumed a lower range between 98° and 101°, and the patient began to make definite progress towards recovery. On November 24th, a course of active immunization with staphylococcus toxoid was begun, and she was discharged from hospital on December 18th with no abnormal neurological signs, and the incision almost completely healed.

A somewhat similar case to the foregoing was that of a woman of 38 years, operated on by Dr. Penfield at the Royal Victoria Hospital, Montreal, for removal of a tumour of the cerebello-pontine angle. Staphylococcal men-



ingitis was diagnosed on the eleventh day after operation. Despite very thorough serum therapy given under the direction of Professor Murray, into ventricle and lumbar space, as well as into vein and muscles, the patient died eight weeks after the operation. At one stage the spinal and ventricular fluids became sterile, and the patient appeared to have a good chance of recovery. But from the outset a very extensive meningitis was present, and the infection was complicated after the second week by an unidentified diphtheroid bacillus.

Three other patients, a boy, a middle-aged woman, and an old man, had a staphylococcal brain abscess drained by Dr. W. Cone at the Royal Victoria Hospital, Montreal. The boy, 8 years old, had been immunized prior to operation with staphylococcus toxoid, and at the time of operation, and subsequently, staphylococcus antitoxin was given intraventrically and intravenously, to protect as far as possible against spread of infection. The post-operative course was uneventful until erysipelas of the scalp developed near the operation wound. This was traced to the fact that during the night the patient took off his bandage and scratched the area, probably to relieve irritation from a serum rash. He died two weeks later of meningitis due to *Streptococcus hæmolyticus*, Type  $\beta$ .

The other two patients, a woman of 34, and a man of 60, were each given 30 to 60 c.c. of staphylococcus antitoxin intramuscularly, prior to drainage of cerebral abscesses proved by preliminary aspiration to be of staphylococcal origin. The former patient during the preceding twelve months had osteomyelitis of the radius, secondary to a furuncle on the forearm with lymphangitis; also pyelonephritis, pleurisy, and later recrudescences of osteomyelitis. The latter patient had been subject to recurrent boils for years, many having lately occurred on the scalp. Dr. W. Cone, under whose care these patients were, at the Royal Victoria Hospital, Montreal, was able to undertake drainage with more confidence knowing antitoxin had been given, and considered that its administration largely accounted for the gratifying post-operative course.

#### PYÆMIA WITHOUT DEMONSTRATED STAPHYLOCOCCÆMIA

In each of the following 3 cases, blood cultures taken on several occasions proved sterile.

A young man, of 19 years, was admitted to

the Victoria Hospital, London, Ontario, under the care of Dr. G. A. Ramsay, acutely ill with signs of osteomyelitis in the region of the left hip joint. There was a history of osteomyelitis of a finger 4 years previously, of nasal obstruction for 6 months, and of a furuncle on the right shoulder 3 weeks prior to admission. Surgical drainage was at once performed, with no resulting betterment. A soft tissue abscess of the left shoulder was drained on the seventh day after the original operation, abscesses of both arms, occipital region, and sternum were opened on the eighth day, and a final abscess near the left elbow on the tenth day. Pus from each abscess grew *Staphylococcus aureus*, while culture of the anterior nasal cavity yielded a pure growth of the same microorganism. Six intramuscular doses of 30 c.c. antitoxin were given six-hourly, beginning on the seventh day, and again beginning on the eleventh day after the first operation, making a total serum dosage of 360 c.c. serum intramuscularly. All the abscesses rapidly healed, no fresh ones developed, and the patient rapidly improved.

A man of 32 was admitted to the Toronto General Hospital, under the care of Dr. J. A. MacFarlane, with an acute finger infection following an injury at work 2 weeks previously. The right little finger had been incised in several places; pus was escaping, and there were signs of deep inflammation over the right shin and left lumbar region. Two days later, a staphylococcal perinephric abscess was drained, after which he ran a high fever for 10 days, with no apparent diminution of toxæmia. On the tenth day, incision was made over the peroneal sheath of his right leg, which was diffusely swollen from knee to toes, and very large quantities of pus were obtained. On this, and the seven succeeding days, 60 c.c. staphylococcus antitoxin were given intramuscularly, a total of 480 c.c., with a view to preventing, if possible, further abscess development and staphylococæmia. No further abscesses occurred and the patient made a good recovery.

The third patient, a boy of 18 years, entered the Royal Victoria Hospital, Montreal, under the care of Drs. Cone and Rogers, acutely ill with nasal blockage, pain and protrusion of the eyeball, and swelling of the right side of face. A very radical drainage operation was undertaken at once, and abundant pus, from which *Staphylococcus aureus* only could be grown, was

encountered in the right frontal sinus, the ethmoid cells, the right peri-orbital tissues, and the right maxillary antrum. During the 3 days following operation, the patient had sweats and chills, temperature ranged from 99 to 104°, there was increasing right exophthalmos, multiple small pustules appeared beneath the skin, and on the third day his hands and arms, body and face, began to twitch. On the same day 10 c.c. of antitoxin were given intramuscularly, followed by 20 c.c. next day. Following this, the boy seemed better, though he began to excrete staphylococci and pus cells in his urine. A further 10 c.c. of antitoxin were then given, and a final 10 c.c. three days later, making a total of 50 c.c. intramuscularly. Dating from the time of commencing serum therapy, the eye swelling and protrusion began to diminish and the temperature to fall; and by the time the last dose had been given, the temperature was normal and antrum washings had become clear. The boy made a complete and rapid recovery, leaving hospital apparently cured only 3 weeks after admission.

#### COMMENTS

By reporting representative case histories, an endeavour has been made to supply evidence authenticating the conviction which contact with a majority of the patients has engendered, that staphylococcus antitoxic serum is a specific therapeutic agent of great efficacy for acute staphylococcal infections and toxæmias, when no staphylococcaemia can be detected by the bacteri-

ological methods currently used. The serum may be given by the intramuscular route without fear of untoward reactions. The dosage required of the antitoxin preparations at present available may lie anywhere between 30 c.c. and 300 c.c. or more, according to the type, intensity and duration of the infection and its associated toxæmia.

Attention is drawn to the fact that of the 4 fatal cases in this series of 40, one patient with a staphylococcal brain abscess died of a fortuitous streptococcal meningitis. Another patient with a very extensive post-operative staphylococcal meningitis showed at one stage, after energetic antitoxin therapy, sterile spinal and ventricular fluids; but eventually died 8 weeks after operation with a diphtheroid bacillus complicating the staphylococcal infection during the last 6 weeks of illness. A third patient, after beginning to make a good recovery from staphylococcal empyema with the help of antitoxic serum, died 8 weeks later from an atypical staphylococcal meningitis of insidious onset, for which unfortunately no antitoxin treatment was given. The fourth fatal case, of staphylococcal arthritis, occurred in a small and distant town, so that cooperation was difficult; and when serum was given, after nearly 2 weeks of acute infection, the patient was already extremely ill.

If these features of the 4 fatal cases be borne in mind, as well as the extreme severity of the toxæmia in many of the 36 other patients in this series who made good recoveries, the results appear particularly favourable.

*(To be continued)*

FATAL DINITROPHENOL POISONING.—M. L. Tainter and D. A. Wood, report a case of death occurring eleven hours following the oral administration of between eight and seventeen times the usual therapeutic dose of dinitrophenol. The dosage taken was estimated, by various methods, to have been at least 2.4, but more probably 5 Gm. The man weighed approximately 80 Kg. (176 pounds), giving an estimated dosage of 62.5 mg. of dinitrophenol per kilogram of body weight. The drug was self-administered with the apparent attempt to produce hyperpyrexia as a therapeutic measure for a supposed syphilis of the central nervous system. The rectal temperature shortly after death was so high that

it could not be recorded by a clinical thermometer, probably being at least 115° F. The onset of rigor mortis was rapid, the body being rigid within ten minutes. A subicteric discoloration of the scleræ and conjunctivæ was present and was due in all probability to the colour of the drug itself. The anatomical changes consisted chiefly in a marked rigor mortis; an acute pulmonary congestion and œdema; ecchymotic hæmorrhages in the endocardium, pericardium and pia; mild nephrotic changes in the kidneys, and a slight detachment of the liver cells from one another. The clinical and anatomical changes bear a striking resemblance to those seen in cases of heat stroke.—*J. Am. M. Ass.*, 1934, 102: 1147.

## THE EARLY DIAGNOSIS OF CANCER OF THE BREAST\*

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## XI.

[T is an unquestionable fact that in the diagnosis and treatment of cancer of the breast the same progress has not been made as in other branches of surgery, as, for example, in perforated duodenal ulcer or appendicitis. There is no statistical proof that cancer of the breast is recognized earlier or that the results of radical operation are better than they were twenty years ago. How is the blame for this deplorable state of affairs to be apportioned? As to the patient, consultation is often deferred because many women have a deep-rooted aversion to a breast examination; others, a natural repugnance to such a mutilating operation as breast amputation; many hide behind the chimerical belief that a tumour of the breast which is painless cannot be of serious moment, while still others fear to know the truth. But there is a grave responsibility resting upon the practitioner. In many instances medical advice is sought early, but, in the absence of typical signs or symptoms of carcinoma, or because the patient is considered young for malignant disease, she is either kept under observation until the diagnosis of cancer is clinically beyond peradventure, or is dismissed with the assurance that there is nothing to worry about. Both of these attitudes are inexcusable. Admittedly, the diagnosis of carcinoma of the breast in its early stages is most difficult, requiring not only large clinical experience but in many cases laboratory aid as well. Yet, once the case has come to consultation, the practitioner must take the responsibility for seeing that a definite diagnosis is made without delay. Thus the ultimate prognosis rests largely in his hands.

In any effort to improve upon the reported results, it is necessary to set out precisely the fallacies which at present have a firm grip upon the lay mind, together with the equally fallacious views held by many practitioners with regard

to the clinical aspects of this condition, and to outline the essentials of an examination. Too often is the examination perfunctory and the opinion given worthless.

For many years I have made a practice of asking each patient admitted to my service who had known of the presence of a tumour in the breast for several months or even a year or more why she had not sought advice earlier, and the reply without exception has been: "Because I had no pain." Each year I have endeavoured to impress upon students the fact that cancer of the breast in its early stages is a painless affection. While it is true that here, as in all clinical fields, one meets with exceptions, these exceptions are found among those cases in which cystic disease is associated with carcinoma; but even in this group, which constitutes from 20 to 30 per cent of all cases of cancer of the breast, pain again is the exception rather than the rule. Tenderness is even more unusual. (Such an exception with regard to both pain and tenderness is cited in Case 3).

It is of course not to be wondered at that the laity should place so much stress upon this feature of pain. In his concept of disease the average person accepts pain as the index of its severity or gravity, and in the more common affections, such as furuncle, caries of the teeth, fracture, pleurisy, appendicitis, biliary and renal calculus, and even the physiological process of parturition, pain is unquestionably the dominant symptom. Less is known by him about the painless affections, such as extensive syphilitic lesions—whether cutaneous, visceral, or cerebrospinal, contracted kidney with general anasarca, and uncomplicated cancer, wherever located. Nor is it a matter of wonder that, in the absence of pain, the practitioner should hesitate to make a diagnosis of cancer, when modern textbooks devote so much space to the discussion of pain as a symptom of this disease. It would be a distinct advance if the authors of the standard texts on surgery would be as silent on the subject of pain in cancer of the breast as is the disease itself, and if the profession, in

\* Earlier articles in the series on the early diagnosis of cancer can be found in the *Journal* as follows:—1933, 29: 465; 1934, 30: 46, 48, 50, 168, 171, 280, 283, 522 and 639.



promoting publicity, would lay greater stress upon the seriousness of painless breast tumours.

With equal vigour must one attempt to combat, both in the lay and the professional mind, the belief, as fixed as that regarding pain, that cancer of the breast never, or but seldom, develops in women under forty years of age. In all large clinics many cases of cancer of the breast are encountered in patients between the ages of 30 and 40; the number of cases met with in patients between the ages of 20 and 30 is by no means negligible; and from time to time one meets with frank carcinoma in the second decade (Case 5). In fact the number of cases recognized in the early years of adult life would appear to be on the increase. In the Mayo statistics on 4,038 cases, reported by Harrington,<sup>6</sup> the largest group (34.8 per cent) occurred between 45 and 54; the next largest group (25 per cent), between 35 and 44.

Another fallacy which must be corrected is the belief that if a visible or palpable tumour is not present a diagnosis of cancer cannot be made. Textbook illustrations of cancer of the breast are confined wholly to advanced lesions, for the simple reason that the hopeful early lesions are not visible. In the early stages there may be no manifestation other than an intermittent bloody discharge from the nipple and a thickened duct; we have had such cases, in which the clinical diagnosis of cancer has been confirmed histologically. The presence of definite thickening in the nipple, with a brownish crust on its surface, the removal of which does not disclose an area of ulceration or cause bleeding, suggests, without any other signs, intrinsic mamillary carcinoma. An erosion on the nipple, however localized, which is not associated with pain or tenderness, but is associated with a thickened duct extending into the breast, is typical of the early Paget lesion. A diagnosis of cancer of the breast, therefore, may be fully warranted despite the absence of the classical signs of a hard tumour, retraction of the nipple, stippling of the skin, and enlargement of the axillary nodes.

The only safe view to engender in the public mind is that any localized non-inflammatory swelling in the breast developing after adolescence may be cancerous; and all women should be urged to familiarize themselves with the normal appearance and feel of their breasts, to submit to a yearly routine examination, and to seek

medical advice at once, should anything abnormal be noted, such as a discharge from or a deformity of the nipple, stippling of the skin, or enlarged axillary glands. For the profession the only justifiable practice is, in all cases, to make a searching clinical examination, and, should there be any ground for doubt as to the nature of the condition, a histological examination as well. To dismiss any patient, of no matter what age, without such an investigation is, in the parlance of the law, to disregard a "warning", which in a certain number of cases will inevitably be inscribed later in the annals of Fate as a "conviction", not only for the patient but for the practitioner as well.

#### METHOD OF EXAMINATION

The patient, stripped to the waist, should be examined in the sitting position and in a good light. Inspection should be first from in front. The size of the breasts, their comparative symmetry, the comparative level of the nipples, and the presence of any visible deformity of either the nipple or the body of the gland, should be noted. One should then stand behind the patient and observe the relative fulness of the breasts from above; and, passing the hand over the shoulder, manipulate and draw out the nipples, noting any difference in pliability or degree of prominence when erect. If there is a crust on the nipple, it should be removed to see if bleeding occurs. Then, by rolling the base of the nipple between the thumb and forefinger, one should ascertain whether there is thickening in the course of any of the ducts and whether blood or serum escapes from the ductal openings. If there is thickening in a lateral duct, the nipple when erect will be tilted toward that side. If there is fixation of all the ducts, the nipple when lifted from its base will show numerous indentations on its surface, corresponding to the duct openings.

Tumours in the body of the gland, whether cystic or solid, are characterized by nodulation, and are generally definitely palpable when the breast is compressed against the chest wall. This method of palpation should be practised in all cases, and both breasts should be examined. In large breasts there may be no evidence of swelling or deformity, and one may be unable to detect a tumour on compression. In such cases careful palpation of the whole breast with both hands, the fingers placed beneath and the

thumbs on top of the breast, may enable one to find a deep-seated growth, which otherwise may escape detection. The patient not infrequently can localize a lesion which the physician fails to find, because she is familiar with the feel of her breasts and very promptly detects any change in their consistence. It is important to determine whether the condition is unilateral or bilateral, grossly or finely nodular, solitary or multiple, cystic or firm, fixed or freely movable.

One should then examine the axilla for palpable axillary nodes.

Finally, transillumination should be done. The essentials are an absolutely dark room and a cold white light, the intensity of which may be varied by a rheostat. The necessary equipment is inexpensive; efficiency in its use comes with practice. To apply this method of examination effectively, one must place the breast between the light and the eye. This method is not applicable to firm, sessile breasts. Transillumination is of special value in differentiating solid from cystic tumours and in detecting in a segment of breast involved in cystic disease areas of opacity due to neoplasia, whether benign or malignant.<sup>2, 3, 4</sup>

#### DIFFERENTIAL DIAGNOSIS

*Fissures of the nipple*, occurring during lactation, are painful and tender and show signs of inflammation, but yield promptly to local treatment if nursing be discontinued. An erosion of the nipple which is not painful or tender but which is associated with a thickened duct extending into the breast, suggests, however localized, the early Paget lesion.

*Cystic disease* may affect one breast alone or both breasts simultaneously, and may or may not be accompanied by pain and tenderness. One or more areas may be involved. The tumour is movable and elastic or fluctuating. There is no thickening of the intra-mamillary ducts, no abnormality of the nipple, no stippling of the skin, no opacity on transillumination. The discharge from the nipple, if any, is serous and not bloody, unless the condition be complicated by papillomatous change. A bloody discharge from the nipple is generally indicative of ductal papilloma, which in 50 per cent of cases is associated with secondary malignant growth. If the duct from which the blood escapes is definitely thickened and indurated, one can be sure that malignant neoplasia complicates the papil-

lomatous lesion. In a previous paper the relation of cystic disease to carcinoma has been fully discussed.<sup>5</sup>

*Cancer*.—In early cancer, as we have seen, there may be no signs apart from bleeding from the nipple associated with a thickened duct or an area of fine nodulation (usually assumed to be cystic), which on transillumination may show an area of opacity; or, without discharge from or deformity of the nipple, there may be an indefinite area of induration, detectable on bimanual palpation, which on transillumination shows as an opacity. These are the early lesions, in which a positive diagnosis can be made only on biopsy. How should this be carried out? The answer is, I feel, only with the patient prepared for immediate radical operation, should the frozen sections prove the tumour to be malignant. In the performance of a biopsy it is safer to excise the tumour widely than to cut into it directly, and the incision should be so placed that it will fit in with whatever incision is visualized as being most suitable for the particular case, should a radical operation have to be done.

In the more advanced stages one recognizes a definite hard tumour, fixed within the breast, commonly associated with retraction of the nipple and either flattening or stippling of the overlying skin. In superficial lesions Cooper's ligaments are, of course, involved earlier than in deep-seated ones; but, including in one group all cases showing skin involvement, we know from experience that in three out of four instances the malignant process has permeated the lymphatic vessels as far as the nearest axillary nodes,<sup>6</sup> whether these are palpable or not; in other words, the disease has already entered upon the third stage or stage of dissemination.

Palpable axillary nodes do not definitely signify metastases; enlargement may be due to a catarrhal inflammation. On the other hand, the fact that no enlargement is noted does not exclude the possibility that metastasis has already taken place; in the Mayo series axillary lymph-node involvement was found at operation in 29 per cent of those cases in which it was clinically not evident.<sup>6</sup>

The advantage of dealing surgically with cancer of the breast before metastases have occurred is strikingly illustrated by the following figures. In the Mayo series<sup>6</sup> of 2231 patients with lymphatic glandular metastases

42.2	per cent lived	3	years after operation;
25	" " "	5	" " "
13.7	" " "	10	" " "

while in their series of 648 patients without lymphatic involvement

77.6	per cent lived	3	years after operation;
66.4	" " "	5	" " "
29	" " "	10	" " "

The following case reports illustrate the text of this paper.

#### CASE 1

Miss E.A.J. (No. W.D.-499-34), aged 57, was admitted on January 24, 1934, under Dr. Guy Johnson, to whom I am indebted for the privilege of reporting the case.

*Complaints.*—Bleeding from the left nipple.

*Personal history.*—Always healthy. Both nipples retracted since childhood.

*Present illness.*—In November, 1933, and again on January 12, 1934, the patient noticed bleeding from the left nipple. She had never had pain or discomfort in the breast.

*Condition on admission.*—Both breasts were very large; both nipples retracted. An indefinite mass was palpable beneath the left nipple, from which blood could be expressed. The axillary lymph nodes were not enlarged.

*Operation.*—On January 25th simple mastectomy was performed, following biopsy and examination of frozen sections.

*Microscopical examination* of whole breast sections showed a depressed nipple, the central duct of which was widened; and 1 cm. from the orifice of this duct was a cystic dilatation containing a papilloma measuring 1 cm. in diameter. The papilloma had a gross connective-tissue stroma covered by a single layer of columnar epithelium. Many of the fronds were fused, presenting an adenomatous appearance. The continuation of this duct and its branches within the breast showed dilatation, thickening of the walls, and atrophy of the lining epithelium, with periductal lymphocytic infiltration, and, here and there, some papillary hyperplasia and desquamation. The remaining breast tissue was atrophic and fatty. Histological diagnosis:—benign duct papilloma.

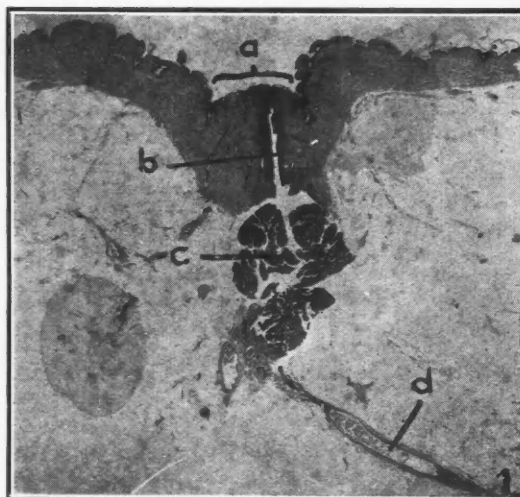


FIG. 1. Case 1.—Photograph of whole breast section (x 2); showing (a) depressed nipple, (b) dilated central duct, (c) benign papilloma in dilated duct ampulla, (d) dilated peripheral duct.

#### CASE 2

Mrs. A.H. (No. 850-34), aged 61, referred by Dr. Drew, of Lachute, was admitted on February 11, 1934, complaining of soreness in the right breast and yellowish discharge from the nipple.

*Present illness.*—In March, 1932, the patient first noticed a crust over the right nipple, which separated as a cap or cast of the tip of the nipple and did not re-form for six months. It again separated in May, 1933. Beneath the crust at this time there was some purulent secretion but no ulceration. The patient applied salve and hot boracic fomentations. Subsequently from time to time the scab partially re-formed, and occasionally there was a purulent discharge beneath it. There had been no bleeding from the nipple at any time. Three weeks before admission the patient noticed shooting pains in the breast, radiating towards the clavicle and the upper and inner part of the right arm.

*Examination.*—The breasts were large, pendulous, symmetrical, with numerous venous markings, more evident over the right. Covering the outer half of the tip of the right nipple there was a very thin epithelial scale, beneath which there was no ulceration. On irritation the nipple became only partially erect. On palpation it was quite firm, as compared with the left, but no extension of this induration into the breast could be made out. Blood could not be expressed. When the nipple was lifted by its base, numerous minute depressions, corresponding to the orifices of the ducts, appeared on the tip, suggesting ductal involvement and fixation. The axillary lymph nodes were not palpable.

*Clinical diagnosis.*—Mamillary carcinoma.

*Operation.*—On February 12th simple mastectomy was performed through a transverse ellipse, with exploration of the floor of the axilla for lymph-gland involvement. None was found.

*Microscopical examination* of whole breast sections showed a glandular epithelial growth occupying the centre of the nipple. The alveoli varied considerably in size. The lumina of the larger ducts were filled with papillary adenomatous masses with multiple points of attachment. There were no Paget cells in the epidermis. *Diagnosis.*—Papillary adeno-carcinoma of low-grade malignancy.

#### CASE 3

Mrs. N.B. (No. 1455-34), aged 35, was admitted on March 12, 1934, complaining of a painful lump in the right breast.

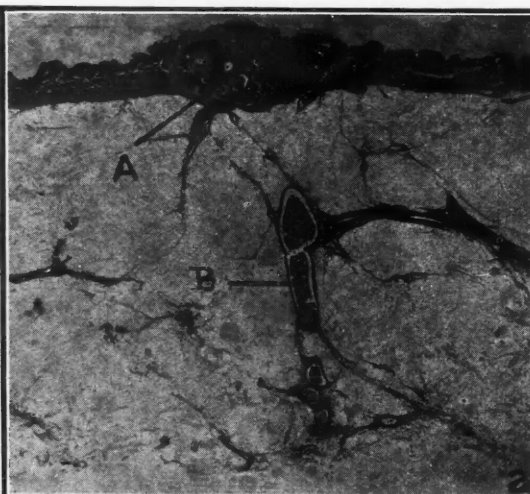


FIG. 2. Case 2.—Photograph of whole breast section (x 2); showing (a) intra-mamillary carcinoma, (b) dilated duct.



*Personal history.*—Married at 13. Nine pregnancies; the eldest child now in his 22nd year and the youngest, aged 3, alone survive. The patient did not nurse any of the children. No history of inflammation or of injury to the breasts. In 1932 she received radium treatment for uterine tumour and did not menstruate again.

*Present illness.*—About January 15, 1934, she noticed a lump in the right breast, associated with slight pain. About the first of March tenderness developed. There was no discharge from the nipple at any time.

*Examination.*—Of under average physique. The breasts were large and pendulous, with a scanty amount of subcutaneous fat. The right nipple was slightly higher than the left and slightly fixed. No ductal induration in the nipple could be made out. In the apex of the upper and outer quadrant, encroaching upon the apex of the upper and inner quadrant, and lying partially beneath the areola, was an irregular, finely nodular mass, about 3 cm. in diameter. This mass was very tender on pressure, and pulling on the nipple caused pain. There was no fixation of the overlying skin. There were no palpable axillary nodes. On transillumination a small, irregular shadow was seen at the outer margin of the nodular mass. *Clinical diagnosis.*—Chronic cystic disease; neoplasia, probably malignant.

*Operation.*—A radical operation was performed.

*Microscopical examination* of whole breast sections through the nipple and tumour showed dilatation of the ducts, but not of the acini. These ducts were lined with flattened epithelium. A few showed small papillary infoldings, consisting of sub-epithelial connective tissue stalks covered with a single layer of columnar epithelium. About many of the ducts is a well marked lymphocytic infiltration. Deep in the breast and some distance from the nipple (at the site where the shadow was seen on transillumination) was a small nodule of typical scirrhous carcinoma, 0.7 cm. in diameter. Surrounding this carcinomatous area was a zone of marked mazoplasia, showing very typically hyperplasia of the periductal and peri-acinal connective tissue. *Histological diagnosis.*—Carcinoma originating in a localized area of mazoplasia. No glandular metastases.

*Comment.*—The finding of carcinoma associated with mazoplasia in this case is, according to Cheatle,<sup>1</sup> most unusual, it being Cheatle's opinion that in a breast which is the seat of mazoplasia there is no tendency to secondary carcinomatous change.

#### CASE 4

Mrs. G. S. (No. 895-34), aged 74, was admitted on February 13, 1934, complaining of a lump in the left breast and bloody discharge from the nipple.

*Personal history.*—Married at 20. Thirteen full term pregnancies; one miscarriage. All the children were breast-fed. No history of injury or infection of the left breast.

*Present illness.*—The patient first noticed a small lump in the left breast one year before admission. This

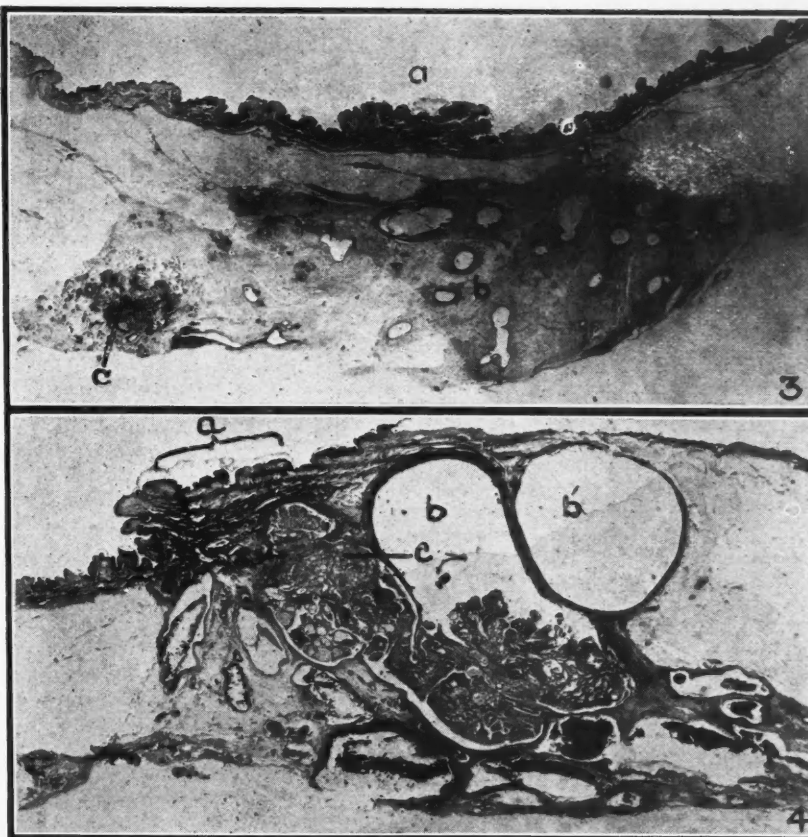


FIG. 3. Case 3.—Photograph of whole breast section (x 2); showing (a) the nipple, (b) numerous dilated ducts, (c) an area of scirrhous carcinoma surrounded by a zone of mazoplasia, the latter characterized by hyperplasia of the periductal and peri-acinal connective tissue.

FIG. 4. Case 4.—Photograph of whole breast section (x 2); showing (a) lateral retraction of the nipple, (b—b') alveolar cysts, (c) papillary carcinoma invading the duct wall.

had gradually increased in size. Three months before admission there was a bloody discharge from the nipple for the first time, and two months later stabbing pain radiating from the breast to the axilla.

*Examination.*—General examination was negative apart from revealing vascular hypertension. The breasts were of medium size and pendulous. In the apex of the upper and outer quadrant of the left breast, lying partially beneath the areola, there was a mass made up of several rounded movable nodules. Of these the largest, about 1.5 cm. in diameter, extended beneath the areola almost to the margin of the nipple, and lay immediately beneath the skin, to which it was not adherent. This mass was definitely fluctuating and, when it was pressed upon, blood escaped from the nipple. At the outer margin of this cystic mass there was a small area of induration, which on transillumination cast a definite shadow. The nipple was tilted toward the tumour and partially fixed. *Clinical diagnosis.*—Cystic disease; malignant intracanalicular papilloma.

*Operation.*—On February 16th a radical operation was performed, without exploration of the tumour. Some enlarged glands were found in the axilla.

*Microscopical examination* of whole breast sections showed the presence of multiple cysts, some of which contained blood. In one of these cysts there was a papillomatous growth, which could be traced medially into a dilated duct, to the walls of which it was attached at many points. The tumour presented a glandular structure with a varying amount of stroma. Some alveoli were large; others, minute. In several areas the connective tissue contained small, closely-packed acini and solid masses and cords of epithelial cells with no

definite basement membrane. There were no Paget cells in the dermis. Sections of lymph glands showed no metastases. *Diagnosis.*—Chronic cystic disease with desquamative epithelial hyperplasia; papillary cystadenocarcinoma of the breast.

#### CASE 5

Mrs. A.G. (No. W.D.—730-33), aged 19 was admitted to the Western Division of the Montreal General Hospital complaining of discomfort in the left breast and was seen by me in consultation with Dr. Albert Ross on June 2, 1933.

*Personal history.*—Married at 16. One full term pregnancy; one miscarriage.

*Present illness.*—The patient stated that for five years she had had a swelling in the left breast, which varied in size but had recently become larger. She had nursed her child (two years old) for several months.

*Examination.*—The breasts were large and symmetrical; the nipples, normal. There had been no bleeding. In the left breast there was an irregular mass, about 1.5 by 1 cm. in diameter, in the upper and inner quadrant, at the margin of the areola, just above the equator. The striking feature was the dimpling of the overlying skin. The mass was fixed in the surrounding breast tissue and quite firm; the surface was smooth.

*Operation.*—With the patient prepared for radical operation resection of the tumour was first performed. The frozen sections showed it to be carcinoma, and a radical operation was then carried out.

*Microscopical examination* showed a circumscribed, non-encapsulated tumour, composed of small, closely-packed acini, lined with cuboidal cells. Throughout the nodule there was a diffuse fibrous tissue stroma. In places the epithelium was arranged in small cords without alveolar formation, these cords extending irregularly into the surrounding fat. *Histological diagnosis.*—Carcinoma of the breast. No axillary lymph-node metastases.

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### PHOSPHATASE IN OBSTRUCTIVE JAUNDICE\*

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PHOSPHATASE is the name given to an enzyme shown to be present in bone and ossifying cartilage by Robison<sup>4</sup> at the Lister Institute. He has demonstrated that this enzyme is intimately related with the process of bone formation. In conditions of generalized bone disease the phosphatase appears to leak out of the bone into the blood in large amounts. Its quantitative determination in the plasma or serum in cases of rickets, Paget's disease, osteitis fibrosa cystica, and in any cases of generalized bone disease is of some diagnostic value.

Phosphatase has recently created considerable interest among the medical profession because of its alleged usefulness as a means of differentiating obstructive from other types of jaundice. Last spring (1933) we made estimations on several specimens of blood obtained from the Toronto General Hospital, some of which were from obstructive jaundice cases, and in these the phosphatase content was found to be higher than normal. Our attention was then drawn to

an article by Roberts<sup>3</sup> from the Sheffield Royal Infirmary. Roberts published his study of 50 consecutive cases of jaundice, reaching the conclusion that "The obstructive nature of jaundice can be recognized by the increased phosphatase activity of blood, which occurs strikingly in this type alone." In view of the fact that such a test would be of great value to the clinician, it was decided to attempt to confirm these findings and, further, to place the work on an experimental basis by the production of jaundice of various types in dogs. The present communication is an account of observations on both clinical cases and experimentally-produced obstructive jaundice; and in addition there are presented for contrast the protocols of the experiments on hæmolytic jaundice, although this phase of the study has just been commenced. The phosphatase was determined by the method to be described in a later issue of this *Journal*, (King and Armstrong<sup>2</sup>); the bilirubin determinations were made by the Thannhauser and Andersen modification<sup>5</sup> of the van den Bergh method.

\* Received for publication June 6, 1934.

### PART I: EXPERIMENTAL OBSTRUCTIVE JAUNDICE IN DOGS

Obstruction to the common bile duct has been produced in 19 dogs, and the serum phosphatase activity and bilirubin have been determined each day following the operation. All the animals sooner or later became definitely ill, exhibiting a typical series of signs. These were lassitude, loss of appetite passing on to complete refusal of food, vomiting, constipation, biliuria and, terminally, marked dehydration. The only therapeutic measure adopted was the giving of intravenous glucose and saline when dehydration became apparent. Only in a few cases was an icteric tint of the skin or scleræ observed. This fact is explained by the great ease with which the kidney excretes bilirubin in this animal.

Relief of the obstruction was attempted in several ways, with only partial success, except in the case of two animals. The reason for this is twofold. Firstly, the common bile duct becomes necrotic and ruptures at the point at which it has been tied off, unless fibrous adhesions grow around it sufficiently rapidly. This can be aided by securing in place a small piece of omentum. Secondly, the animal is in very poor physical condition by the time the second operation is performed, since the liver is badly damaged by the back pressure. Infection takes place very rapidly, and in addition to those dogs dying from peritonitis a few have died from bronchopneumonia.

In order to conserve space a composite chart of the phosphatase activity in the serum of ten dogs following complete obstruction to the common bile duct has been compiled, and a general description of these animals will be given. More in detail, however, the results of three other experiments will be described. In two of these after a period of some days the obstruction to the flow of bile was removed, and the animals recovered completely. The remaining case, although the dog finally died, is instructive, since it combines the effect produced on relief of obstruction, first, when the phosphatase is at a medium height, and later, when the value is exceedingly high.

1. *Obstruction of the common bile duct.*—The common bile duct was dissected out under ether anaesthesia in ten dogs. The duct was then either cut and ligatures applied to the cut ends, or it was tightly tied in two or more places and

left uncut. The animals were then placed in metabolism cages and observed for from 4 to 6 days. They were supplied with food and water each day, but no therapeutic measures were applied. Blood was withdrawn from the femoral vein prior to the operation and on each succeeding day for estimation of phosphatase and bilirubin. In Chart I units of phosphatase in

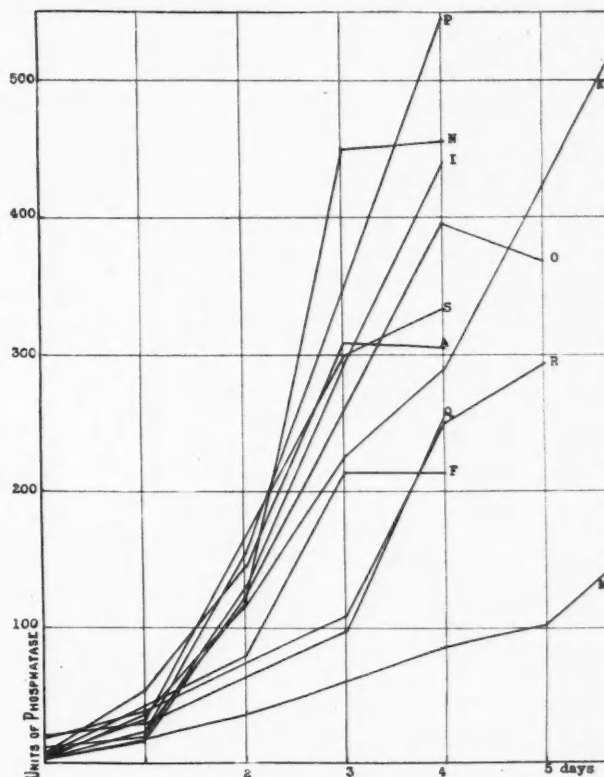


CHART I.—Units of serum phosphatase in dogs after obstruction of the common bile duct.

the serum have been plotted at daily intervals for each experiment. On the day following operation the majority of the dogs had recovered satisfactorily and were taking food. In a few cases bilirubin was present in the urine. In all cases there was a definite increase in serum phosphatase (10 to 50 units). The van den Bergh reaction was negative. On the second day they all appeared to be quite well. The urine, however, invariably showed the presence of bilirubin and continued to do so on succeeding days. Bilirubin could now be detected in the serum and was always present from then on. The serum phosphatase had increased very markedly (a further 20 to 85 units). By the third day most of the dogs were refusing some of their food. A further marked increase in serum phosphatase was present, the value being in the majority of cases over 200 units. On the fourth day the animals were drowsy and fre-



quently appeared acutely ill. An icteric tint was visible in the sclerae and mucous membranes. In only one case was the phosphatase value below 200, while one animal reached the height of 545 units. Only three dogs were observed in the obstructed state until the sixth day, and in these the clinical picture became more pronounced, while the phosphatase continued to rise. The remaining dogs died of bile peritonitis either before or after an attempt was made to relieve the obstruction.

It will be noticed on reference to Chart I that four of the curves fall off slightly, or fail to rise higher after the third and fourth days. This fact was associated with the finding at autopsy or laparotomy that the duct had ruptured at the point of ligature.

Gall-bladder bile was obtained at autopsy on a number of these animals and the phosphatase activity per 100 c.c. was estimated. The following values were obtained:

Dog	Units of phosphatase per 100 c.c. bile
F .....	819
I .....	138
K .....	227
M .....	410
O .....	750
Q .....	394
R .....	1710

The autopsy findings were in general the same for all dogs. The bile ducts and the gall bladder were markedly dilated; except where rupture had occurred they contained a large amount of bile under tension.

## 2. Obstruction of the common bile duct followed by relief of obstruction.—

### Experiment 1.—A large mongrel police dog.

Under morphine and ether anaesthesia the common bile duct was dissected out for a distance of 2 cm. from the intestinal end. A small wire paper clip, bent so as not to be too tight, was slipped into place. This produced obstruction not only by pressure but also by virtue of its bending the duct on itself. Pressure was now made on the gall bladder and it was seen that the duct became dilated above the clip, and that apparently none of the bile could pass beyond this point. A silk thread was then tied to the clip. The wound was closed leaving the other end of the thread beneath the muscle layer.

The serum phosphatase and van den Bergh reaction are shown graphically in Chart II(a). The latter value has been multiplied by 10 before plotting, in order to give it greater significance on the same scale as phosphatase.

The initial phosphatase was 4.5 units. After the operation the rise was slow, but definite. On the third

day the animal was still apparently quite well. The phosphatase value lay at 106 units, while the van den Bergh reaction could just be read (0.4 units). The urine was bile-stained. Under morphia and ether anaesthesia the wound was now re-opened. The abdomen was free from peritonitis. Adhesions in the region of the gall bladder were carefully broken down and the clip exposed. By steady traction it was removed. No leakage of bile was observed. The abdomen was closed again. On the following day a marked drop in phosphatase had occurred; the van den Bergh reaction was negative, but bilirubin was present in the urine. In the course of 20

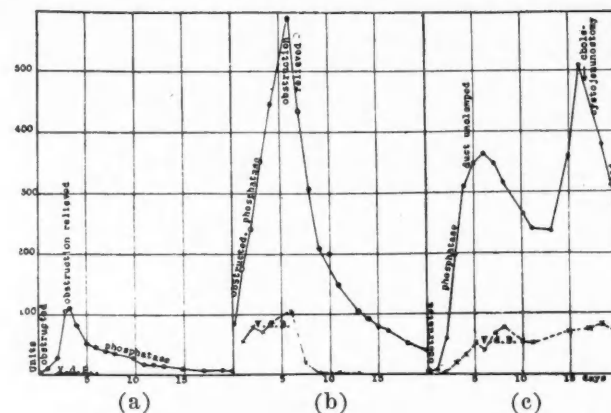


CHART II.—Units of serum phosphatase and bilirubin (van den Bergh x 10) after obstruction to the common bile duct in dogs.

days the phosphatase fell continuously and reached finally the initial level. The urine became negative for bilirubin on the eleventh day. During the early stages of recovery the animal suffered from mild diarrhoea.

### Experiment 2.—A large pack hound.

Obstruction of the common bile duct was produced in a second dog in the same manner as before. When the duct was exposed an unusual condition was encountered, namely, the duct was seen to be dilated and contained bile under slight pressure. It did not occur to us at the time that this represented other than the physiological emptying of the gall bladder at that moment. However, when the initial phosphatase determination was made it was found to be very high (88 units). Unfortunately, the van den Bergh reaction was not carried out on this first blood sample, but on the next day it had reached 6 units. (This is much higher than can be obtained by a single day's obstruction).

Chart II(b) shows the phosphatase and van den Bergh units graphically from day to day. The response to the experimental obstruction was very marked as regards phosphatase, the activity of the serum by the sixth day being 592 units. The van den Bergh reaction reached 10.5 units by this day, and an icteric tint to the sclerae was evident as early as the fourth day. The urine was not observed until the second day, when it was found to contain a large amount of bilirubin.

On the sixth day it was decided to remove the clip in view of the fact that the dog was refusing food and appeared acutely ill. A slight discharge was present in the nose. For this reason the abdominal wound was opened under morphia and a local anaesthetic (novocaine). There was no evidence of any peritonitis and the clip was removed without difficulty. Recovery was good, clinically, and the nasal discharge rapidly disappeared. By the fifteenth day the icteric tint was scarcely visible in the sclerae. The phosphatase had fallen to 21 units on the thirtieth day, and the van den Bergh reaction had been normal for some time. During the early recovery stage the stools were loose and deeply pigmented.

*Experiment 3.*—A large police dog.

The obstruction in this animal was produced in such a way that it could be relieved by unclamping a pair of forceps which kept tight a rubber band around the duct. The handles of the forceps were left in the wound under the skin. After four days the signs of obstruction were well marked, and the serum phosphatase had reached a high level (315 units). The forceps were now unclamped. After a lag of two days clinical improvement was noted, and this corresponded to a fall in serum phosphatase to 235 units. On the sixteenth day, however, the animal was again becoming very ill, and, as can be seen by reference to the chart, the serum phosphatase was at this time rising rapidly and reached 515 units. Cholecysto-jejunostomy was performed on the twentieth day, following which a marked fall in phosphatase content occurred (to 280 units). Unfortunately, the animal died two days later. Autopsy revealed a very marked dilatation of all the bile ducts and an intense peritonitis. The point at which obstruction had been produced was stenosed by fibrous adhesions. Gall-bladder bile obtained at autopsy contained 962 units of phosphatase in 100 c.c. of bile.

3. *Experimental hæmolytic jaundice.*—Owing to the rapidity of excretion of bilirubin by the kidney in dogs we have so far been unable to produce clinical jaundice by the hæmolytic agents employed; nor have we been able definitely to obtain a positive van den Bergh reaction in the serum, although it is quite easy to cause bilirubin to appear in the urine in large amounts. When such amounts of bilirubin are thus excreted, it is probable that had the same degree of hæmolysis occurred in a human being, clinical jaundice would have occurred. On the other hand, the experiments are inconclusive, since it might be argued that failure of the serum phosphatase to rise appreciably under such conditions is directly related to the absence of bilirubinæmia. The experiments are therefore presented only as preliminary observations.

Hæmolysis has been produced in two ways: (1) 100 to 200 c.c. of blood were removed from the animal, laked in water, strained through a sterile towel, and re-injected into a vein; (2) 1 per cent sodium oleate solution was injected intravenously on successive days.

## DISCUSSION

In all of the nineteen animals examined following obstruction there was a rapid and pronounced rise in serum phosphatase. The rapidity of the rise and the height reached varied from one individual to another. After five or six days the value was at least thirty times the normal, and in some cases as much as one hundred times. The rapidity of the rise is no doubt governed in some degree by the elasticity of the gall bladder and by the amount of bile in it when the obstruction is produced.

In the cases in which we have been able to relieve the obstruction without losing the animal, two types of response have been noted: one an immediate and marked fall in the phosphatase activity (100 units or more in a day); the other a slowing up of the rise, then a plateau, and finally a slow fall towards normal. This latter response we have reason to believe is associated with cases in which there is marked damage to the liver cells.

Protocols of 3 such experiments are as follows.

*Experiment 1.* A fox terrier, weighing 7 kilos.

Day	Treatment	Plasma Phosphatase	Hunter's test for Bilirubin in Urine	Clinical Condition
0	Anæsthetized with ether. 100 c.c. blood removed, laked in 100 c.c. water, 0.9g. NaCl added, strained through towel, the whole re-injected.	3.5	Negative	Healthy.
1	—	6.9	Positive	Anorexia.
2	—	12.7	Negative	Refused all food.
5	—	9.5	Negative	Refused all food.
6	—	7.8	Negative	Refused all food.
8	—	7.2	Negative	Return of appetite.
16	—	4.4	Negative	Quite well.

The van den Bergh reaction (indirect) was just noticeable one day after the injection, while the urine contained a large amount of reddish purple pigment. The hæmoglobin on the same day had fallen 12 per cent, but returned to normal on the following day.

*Experiment 2.* A small Boston bull, weighing 10 kilos.

Day	Treatment	Plasma Phosphatase	Hunter's test for Bilirubin in Urine	Clinical Condition
0	100 c.c. blood removed, laked in 200 c.c. water, filtered through towel, re-injected.	9.2	Negative	Sudden collapse, vomiting, and voiding of urine & fæces, with rapid recovery during injection.
1	—	11.8	Positive	Quite well.
2	—	12.4	Positive	" "
4	—	10.8	Negative	" "
7	—	10.0	Negative	" "
15	—	8.4	Negative	" "

The van den Bergh reaction was negative throughout the experiment. A slight fall in hæmoglobin was encountered one day after the injection, followed by a rapid return to normal. On the same day a reddish purple pigment was present in large amounts in the urine.

*Experiment 3. A fox terrier, weighing 10 kilos.*

Day	Treatment	Plasma Phosphatase	Hunter's test for Bilirubin in Urine	Clinical Condition
0	50 c.c. 1% sodium oleate intravenously	8.2	Negative	Quite well.
1	"	8.5	Strongly positive	" "
2	"	10.6	Positive	" "
3	"	12.6	Positive	" "
5	"	10.7		" "
6	"	11.3		Left fore-limb swollen at site of injection.
7	"	12.2		Left fore-limb swollen at site of injection.
9	Injection stopped	9.4	Positive	Refusing all but a little food.
10		8.7	Positive	Nasal discharge.
12		7.8		" "

From the 1st to the 14th day the hæmoglobin slowly fell from 92 to 56 per cent. Bilirubin was present in the urine whenever examined. The van den Bergh reaction of the serum remained negative throughout.

Other investigators have been aware that bile contains some phosphatase. However, the amounts were considered to be small. Difficulties were encountered by these other workers in applying their methods to the estimation of bile phosphatase, whereas the method used by us is remarkably suitable for work with bile. Bile taken from animals, either at operation, at autopsy, or from a biliary fistula, was examined. The results for bile given above indicate that gall-bladder bile contains large amounts of phosphatase after obstruction to the common bile duct (av. 635 units). It was at first thought, therefore, that small amounts of phosphatase were excreted daily by the liver and that during obstruction the enzyme became concentrated in the bile. However, using bile-fistula animals with no obstruction, we found that as much as 5,000 units per 100 c.c. were being excreted daily for several days, the total amount of bile varying from about 50 to 125 c.c. Thus the present indication is that large amounts of phosphatase are excreted daily into the bile and that the excretion diminishes or ceases when obstruction to the bile ducts is produced, and, since the producing mechanism has presumably not been damaged, the amount of enzyme in the serum rises.

In view of the enormous amount of phosphatase excreted in bile it seemed advisable to examine the fæces. In normal dog fæces even

much greater amounts of enzyme were found present than in bile. After obstruction to the common bile duct, no marked change in the phosphatase content of the stools was observed. The fæces of only two animals have been tested during obstruction to the flow of bile, and thus we are not prepared to make further comment on this finding at the present time. It may be pointed out that a high content of phosphatase exists in and is presumably elaborated by the intestinal mucosa, and that various bacteria manufacture the enzyme. The fæces phosphatase may come in part from both these sources. The urines of obstructed animals were tested for phosphatase, but we were unsuccessful in demonstrating its presence.

The increased production and excretion of bilirubin caused by experimental hæmolysis is unaccompanied by any change in serum phosphatase activity comparable to that found in the obstructed cases. There is, it is true, in each of the three cases evidence of a slight increase in the value, but we do not look upon this as significant without further corroboration. Such a change might represent mild liver damage brought about concomitantly with the hæmolysis, especially in experiment 3 when sodium oleate was administered. In a future paper it will be shown that toxic damage to the liver cells gives rise to definite increases in serum phosphatase.

## PART II: CLINICAL OBSTRUCTIVE JAUNDICE

The opportunity to follow several proven cases of obstructive jaundice in the wards of the Toronto General Hospital has been utilized to determine the value of serum phosphatase before, during, and after the occurrence of obstruction of the common bile duct. Brief abstracts of their clinical histories follow.

## CASE 1

W.A., aged 60, was admitted to the surgical wards on January 29, 1934, complaining of loss of weight (50 pounds), loss of strength, pain in the left side, diarrhoea, jaundice of three months' duration and slowly increasing intensity. The stools were clay-coloured. Examination showed intense jaundice (van den Bergh 30 units); liver enlarged to umbilicus, but not tender; numerous ecchymoses; no masses were felt in the abdomen. A pre-operative diagnosis of carcinoma of the head of the pancreas was confirmed at operation on January 30, 1934. The gall bladder was anastomosed to the stomach. This was followed by rapid subsidence of the jaundice and hæmorrhages. The first phosphatase estimation was made when he was transferred to the surgical wards January 29, 1934, and gave the high value of 162 units. Following operative relief of the obstruction the serum phosphatase fell rapidly. Its fall was paralleled by a similar fall in the intensity of the van den Bergh reaction and coincided with the subsidence of the jaundice (see Chart III).



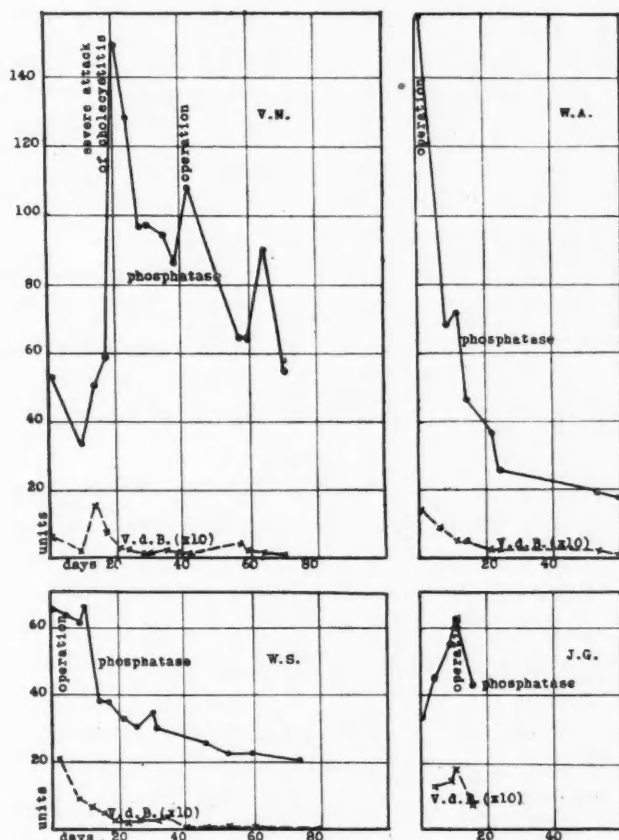


CHART III.

## CASE 2

W.S., aged 46 years, was admitted on January 25, 1934, with the following history: upper abdominal pain (one brief but severe attack three months before admission); jaundice of three months' duration increasing in intensity; intense itching of the skin, clay-coloured stools, and loss of 45 pounds in weight. Examination revealed intense jaundice (van den Bergh 30 units), great enlargement of the liver (below umbilicus), marked pruritus. Operation on January 30, 1934, revealed a small hard mass in the head of the pancreas, great dilatation of the biliary tract and of the gall bladder. No stones were felt. It was not possible to determine whether the pancreatic mass was carcinoma or chronic pancreatitis; a cholecystogastrostomy was performed. The intense itching disappeared in twenty-four hours. The jaundice diminished slowly but steadily. By March 30th he was greatly improved; jaundice had almost completely disappeared; he had gained 25 pounds in weight, and the liver had diminished in size. The first serum phosphatase estimation was made on January 26, 1934—65 units. Following operation the figure fell slowly for a week and then more rapidly. There was a coincident, but more rapid, fall in the van den Bergh reaction. During the same period the jaundice faded (see Chart III).

## CASE 3

V.N., aged 44 years, was admitted on February 23, 1934, with a history of recurring attacks of biliary colic. An attack in September, 1933, was accompanied by jaundice. Her present attack was of five days' duration, and jaundice had been present for three days. Examination showed moderate jaundice (van den Bergh 5.8 units); no fever; the liver, enlarged but not tender; the gall bladder, enlarged and tender. The spleen was considerably enlarged. Though the history and physical findings were those of recurring attacks of cholecystitis and common duct obstruction, the enlarged spleen introduced the possibility of Banti's syndrome. She had been

born in the Balkans and presumably exposed to malaria. Her condition was carefully investigated during a period of six weeks. In this time she had a severe attack of cholecystitis with great enlargement of the gall bladder, fever and leucocytosis. Operation on April 10, 1934, revealed a large gall bladder surrounded by recent adhesions, filled with stones, and stones in the common duct. The gall bladder was removed and the common duct drained with a T tube. The serum phosphatase on admission was 54 units. It fluctuated about this level until her severe attack of cholecystitis during the period of observation, and then rose sharply to 148 units. At the time of operation it was 108, and by May 7th it had fallen to 55.

## CASE 4

J.G., aged 59 years, was admitted on February 14, 1934, with a large carcinoma of the stomach and nodules in the liver. On February 19, he became jaundiced and this condition rapidly deepened. Operation performed on March 1, 1934, revealed a large carcinomatous mass in the head of the pancreas obstructing the common bile duct. There were numerous secondary nodules in the liver. The gall bladder was drained. He died on March 5, 1934. Serum phosphatase on the day jaundice was first noted was 36.7 units and this rose to 61 units as the jaundice deepened. It fell after operation to 43 units (see Chart III).

## CASE 5

J.C., aged 54 years, was admitted on March 8, 1934, for recurring attacks of pain in region of gall bladder; a severe attack in October, 1933, since which time there had been more or less grumbling pain. Two weeks prior to admission the pain had become more severe, and on March 5th she developed intense pain, with vomiting. Examination on admission revealed slight jaundice; temperature 101.4° F.; white blood cells 12,800; the abdomen was distended, tender and rigid in the region of the gall bladder; liver three fingers' breadth below the costal margin; gall bladder palpable and tender. The diagnosis was made of acute cholecystitis with stones, and partial obstruction of common duct, either by stone or oedema. She was treated conservatively with some improvement. Her condition fluctuated from time to time without ever completely clearing up. Fever was constantly present. April 11th her condition was worse and operation was undertaken. This revealed an inflamed gall bladder which had perforated. Stones were present in the gall bladder cystic duct, and several were impacted in the common duct. Bile peritonitis was present. She died on April 15, 1934, and autopsy revealed, in addition to the operative findings, an extensive suppurative cholangitis with an abscess in the left lobe of the liver. During the course of her obstructive jaundice the phosphatase and van den Bergh reaction were constantly high (serum phosphatase 60 to 182 units; van den Bergh 9 to 28 units) (see protocol).

## PROTOCOL—CASE OF J.C.

Date	Day	Serum phosphatase	van den Bergh
March 9	0	17	9
" 14	5	59	21
" 19	10	81	9
" 21	12	182	21
" 26	17	101	21
April 5	27	87	25
" 12	34	106	28

These five patients are proved examples of obstruction to the common bile duct in which the serum phosphatase was followed by numerous estimations either during the development

of the jaundice (as in the case of J.G.) or during the subsidence of the jaundice (as in the other four cases). In all the obstructive jaundice was accompanied by a great rise in the serum phosphatase, which roughly paralleled the intensity of the jaundice. To date, these represent all of the cases of obstructive jaundice we have been able to follow continuously, and at the same time demonstrate the nature of the jaundice. A number of isolated observations on proved jaundice cases confirm the belief that obstructive jaundice is accompanied by a marked rise in the serum phosphatase.

No cases of frank hæmolytic jaundice were available in the Toronto hospitals at the time this part of the study was undertaken. We were fortunate, however, in obtaining blood from two cases of latent hæmolytic jaundice. A single estimation on the blood of each of these cases yielded the following values.

Name	Age	Serum phosphatase per 100 c.c.	van den Bergh
B. (M.)	27	7.2 units	2 units (indirect)
L.		7.8 units	1.7 units (indirect)

The normal phosphatase value for adults by the method employed lies within the range 3 to 13 units, so that no appreciable rise has occurred in these two cases. This fact is in agreement with the observations reported on dogs.

#### SUMMARY

1. Obstruction to the common bile duct has been produced in 19 dogs and the serum phosphatase activity and bilirubin content determined daily.
2. The serum phosphatase in every case rose to progressively higher values each day fol-

lowing the obstruction, reaching thirty to one hundred times the initial amount after six days.

3. In two cases the obstruction was later relieved and the animals allowed to recover. The recovery period was accompanied by a fall in the serum phosphatase until the initial value had been reached.

4. Gall bladder bile contains large amounts of phosphatase, while bile from a fistula has been noted to contain even greater amounts.

5. Fæces from the dogs before and after obstruction possessed very great phosphatase activity.

6. Five hospital cases of proved obstructive jaundice were followed daily in regard to the serum phosphatase activity. During the development of jaundice the serum phosphatase increased from day to day, while during the subsidence of the jaundice the value diminished, although somewhat more irregularly. When the patient recovered it reached very nearly the range given by normal individuals.

7. The height to which the phosphatase activity rose in the human cases was considerably less than that attained in dogs.

8. Three cases of experimentally produced latent hæmolytic jaundice in dogs and two cases of latent hæmolytic jaundice in humans were investigated. No appreciable rise was observed in serum phosphatase.

We wish to express our thanks to Dr. F. G. Banting for his advice and constructive criticism while this work was being carried out.

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ALLERGIC REACTION TO DINITROPHENOL.—Gerald M. Frumess stresses the fact that alpha-dinitrophenol produces skin eruptions in a large percentage (at least 7 per cent) of those to whom the drug is administered. These eruptions occur when non-toxic amounts of the drug are used. Some of these eruptions are definitely allergic, specific antibodies being produced in some individuals by the ingestion of the drug. In at least one case, these antibodies were demonstrable by the Prausnitz-Küstner passive transfer test. It is theoretically dangerous to resume the use of the drug after a skin

reaction from its ingestion has subsided.—*J. Am. M. Ass.*, 1934, **102**: 1219.

Man is a dupeable animal. Quacks in medicine, quacks in religion, quacks in politics, know this and act upon this knowledge. The credulity of man is unfortunately too strong to resist the impudent assertions of the quack. Credulity has been justly defined as belief without reason. It diffuses itself through the minds of all classes, by which the rank and dignity of science are degraded, and its valuable labours confounded with the vain pretensions of empiricism.—Southey.

## SILICOSIS AND THE METABOLISM OF SILICA

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**SILICOSIS** is an industrial disease arising from the entrance of finely particulate silica into the lungs of workers in dusty trades. The presence of large amounts of silica in the lungs leads to the production of extensive nodular fibrosis. It is the purpose of this communication to present the results of a study of the metabolism of silica when introduced into the body in a variety of ways, and the means which the body has at its disposal for the elimination of silica.

In previous studies from this laboratory<sup>1, 2</sup> attention was drawn to the fact that all body tissues and fluids, whether fetal or adult, showed the presence of significant amounts of silica when examined by a delicate colorimetric method of analysis. Whether or not silicon should be considered an essential constituent of animal protoplasm cannot at present be decided. Its universal presence appears reasonable, however, when one remembers that it is always a constituent of the environment of the developing egg, whether that environment be the water of the ocean or the blood of a mammalian mother.

The paths of entry for silica into the body are, of course, the digestive tract and the lungs. The most of that entering the gut is eliminated in the faeces, but a fairly large amount must be absorbed into the blood, as is shown by the constant excretion of silica in the urine, particularly in the case of herbivorous animals which are ingesting large amounts in their food. All foods of vegetable origin contain silicon, the hulls of grains, hay and straw being particularly rich in this element.<sup>3</sup> That there is little retention of this absorbed silica in the body is indicated by the relatively low silica content of the liver, spleen and kidneys of these animals.

That the silica content of the urine may be influenced at will by the diet was shown by an experiment in which four rabbits, which had been kept on whole oats and carrots, and which showed a high silica content in the urine, were placed for four weeks on a white bread and tomato juice diet; the urinary silica values began

to drop immediately the change of diet was made, and continued low until the animals were put back on oats and hay, when the amounts excreted in the urine rose very markedly (Chart 1).

The administration of pure silica into the

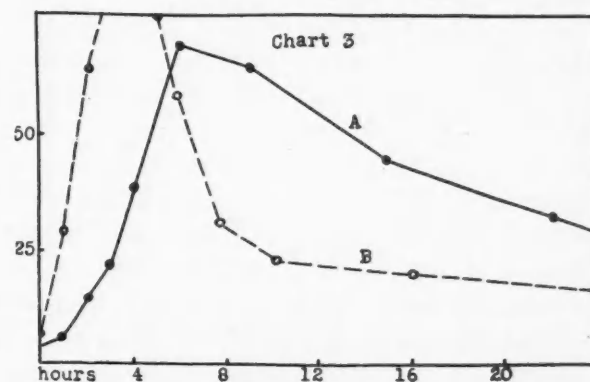
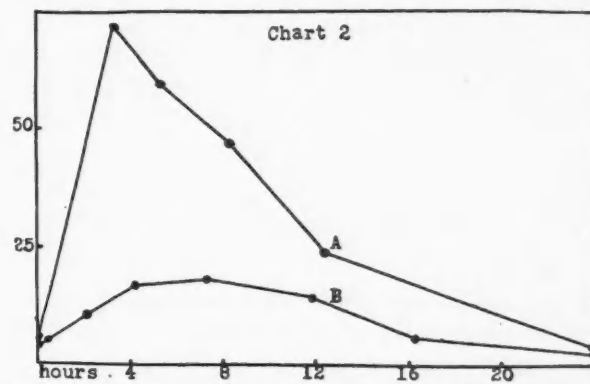
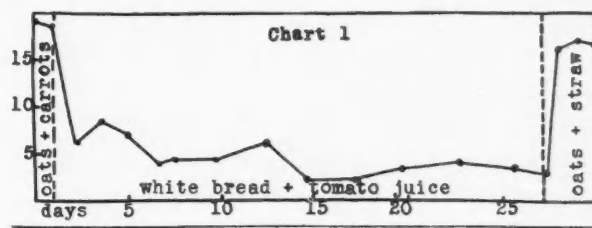


CHART 1.—Influence of diet on the urinary excretion of silica in rabbits.

CHART 2.—Effect of administration into the dog's stomach (A) of silicic acid, and (B) of powdered quartz, on the excretion of silica in the urine.

CHART 3.—Effect of silicic acid injected into the blood stream on the excretion of silica in the urine. (A) 150 mg. injected during 6 hours; (B) 200 mg. injected during 5 hours.

The figures on the left represent mg. SiO<sub>2</sub> per 100 c.c. of urine.



stomach, whether as silicic acid or as powdered quartz, was also followed by a prompt increase of the content of silica in the urine (Chart 2). The increases were, naturally, more marked when the soluble silica was used (silicic acid) than when the insoluble form was given. It would appear that whatever silica enters the blood by way of the intestine passes rapidly into the urine, there building up to high concentration without any demonstrable increase in the silica concentration of the blood.

Several experiments were conducted in which soluble silica was introduced into the blood stream by continuous intravenous injection over periods of several hours (Chart 3). The urinary excretion of silica promptly rose from small initial amounts to high values within the first hour, and very high concentrations of silica were found in the urine toward the end of the period of injection. The level of silica in the blood was raised during this time to only a very minor extent when compared with the increases in the urine. These experiments appeared to indicate that the body possesses a very efficient mechanism for the disposal of silica, once it has entered the blood stream in the soluble form. The existence of a low kidney threshold for silicate was thus demonstrated.

The entrance of silica into the lungs is brought about by the inhalation of finely particulate silica dust. Miners, sand-blasters, and many other workers in dusty trades are subject to the presence of large quantities of silica in the air they breathe; even in normal individuals seldom exposed to dusty conditions a considerable amount of particulate silica must enter the lungs.

Of the silica dust inhaled, the majority of the particles are wafted up by the cilia of the bronchial epithelium and are either expectorated or swallowed, but the finest of the particles find their way into the alveolar spaces, and once they have lodged in the parenchyma there is no ready means of exit. Some particles which are engulfed by phagocytic cells which have passed into the air spaces are expectorated with their enveloping cells; other ingested particles are drawn into the lung parenchyma, and the migration of the phagocytes carries them varying distances in the lymph channels. That many particles reach the lymph nodes, and even the spleen by way of the blood stream, is attested by the high silica content of these glands.<sup>1</sup> The

finest of the particles may, however, be slowly dissolved by the mildly alkaline body fluid constantly bathing them, to be carried away in solution and excreted in the urine.

Former experiments by the authors,<sup>2</sup> and by Kraut<sup>4</sup> showed an increase in the urinary output of silica following the spraying of neutralized sodium silicate solutions into the lungs, but the increases noted may have been due to expectoration and swallowing of the solution followed by absorption into the blood from the gut. Experiments have now been completed, however, which demonstrate absorption from the lung with no possibility of the silica reaching the blood by way of the intestine. Under amytal anaesthesia the oesophagus of a dog was exposed and was clamped off by means of artery forceps, the prongs of which had been bent so as to exert only a gentle pressure. A bronchoscope was inserted through the trachea into the left bronchus, and the dog was then raised into a vertical position. Fifty c.c. of silica-containing solution (soluble or particulate) were now allowed to run slowly down into the lung through a narrow tube passed down the bronchoscope. Thorotrast was mixed with the silica solution,

TABLE I.

## URINARY EXCRETION OF SILICA WHEN ADMINISTERED INTO THE LUNG.

Amytal anaesthesia; oesophagus clamped off with artery forceps.

*Dog 27:* silicic acid solution (60 mg.  $\text{SiO}_2$ ) introduced into the left lung.

Hours	Mg. $\text{SiO}_2$ per 100 c.c. urine	c.c. urine	Total $\text{SiO}_2$ excreted in the urine
0	1.8	—	—
2	44.2	20	8.8
4	47.4	14	6.6
7	29.4	17	5.1
Night	28.1	66	18.6
25	28.0	1	0.3
Total $\text{SiO}_2$ recovered =			39.4 mg.

*Dog 29:* 50 c.c. of quartz suspension (0.5 g.  $\text{SiO}_2$ ) introduced into the left lung.

Hours	Mg. $\text{SiO}_2$ per 100 c.c. urine	c.c. urine	Total $\text{SiO}_2$ excreted in the urine
0	1.1	—	—
3/4	5.4	19	1.0
3	12.0	14	1.7
5	8.6	8	0.7
7	11.2	16	1.8
Night	6.9	40	2.8
25	5.4	4	0.2
Total $\text{SiO}_2$ recovered =			8.2 mg.

and an x-ray photograph taken as soon after administration as possible, to determine into which areas of the lung the solution had penetrated. Catheter specimens of urine were taken immediately before the administration and at intervals afterwards. These samples were measured as to volume and to silica content by the colorimetric procedure described in the protocols.

The results of two experiments are given in Table I. In the first (where soluble silica was used) a very marked increase from 1 to nearly 50 mg. per cent of silica in the urine took place. In the time during which the urinary silica was followed a total of 40 mg. was excreted. If it be assumed that this silica came entirely from the silicic acid placed in the lung, then 66 per cent of that administered was recovered in the urine. Lesser increases were observed in the second case where a very finely particulate suspension of quartz dust (made by water sedimentation of powdered quartz) was employed. As might be expected, there was not so great a rise in the output of silica in the urine as in the case where soluble silica was administered. During the twenty-four hours the dog was kept under the anaesthetic a urinary silica level of about ten times the original was maintained. A total of 8 mg. was recovered, which is a little less than 2 per cent of the half gram of silica administered. This 2 per cent probably represents the very finest of the particles in the sample given. It is believed that these increases indicate a capacity on the part of the body fluids circulating in the lung to dissolve silica even when it is present in the form of the highly insoluble crystalline fragments of quartz. The rate of solution is, of course, a function of the size of the particles with which the dissolving fluid is in contact, and in this experiment the finest particles obtainable from a quartz dust, prepared by sedimentation after prolonged grinding in a ball-mill,\* were used. The majority of the particles were under three microns in size.

In the case of human beings it is probable that large numbers of extremely fine particles, smaller even than the very fine particles observable under the microscope in the lungs of individuals exposed to a dusty atmosphere, are

constantly finding their way into the lung. In contact with the fluid in the lung these smallest of particles may suffer fairly rapid solution, the larger particles slower and only partial solution. In this way there may be a constant drainage of silica from the lung, the dissolved silica being carried away by the blood to be excreted in the urine.

Having gained some knowledge of the metabolism of silica from animal experimentation, it was considered advisable to test the urine of a group of miners exposed to silica dust. Through the courtesy of Dr. W. D. Robson, the authors were allowed to collect 58 specimens of urine from underground workers in a mine at Schumacher. The men came direct to the mine dispensary from the changing-room, and were each asked to void a specimen of urine in a Bakelite test tube fitted with a rubber stopper. Analysis of the samples was made a few days later in the laboratory at Toronto. The results are set forth in Table II. It will be seen that the values in milligrams per 100 c.c. of urine vary all the way from less than 1 to nearly 6.

TABLE II.  
SILICA CONTENT OF THE URINE OF GOLD MINERS

No.	Specific gravity	Mg. SiO <sub>2</sub> per 100 c.c. urine	No.	Specific gravity	Mg. SiO <sub>2</sub> per 100 c.c. urine
531	1.018	1.6	134	1.023	1.7
363	—	5.6	M.	1.007	1.1
309	1.023	3.0	61	1.027	3.4
178	—	3.5	301	1.014	1.6
762	1.010	1.8	101	1.029	1.9
99	—	4.0	540	1.024	1.8
155	—	1.3	1558	—	2.9
208	1.028	1.2	65	1.028	2.8
197	1.025	—	75	1.021	1.7
226	1.026	2.0	754	—	3.0
483	1.028	1.7	331	—	1.4
148	—	1.0	185	—	2.4
763	1.029	3.6	A.	—	2.7
407	1.026	1.4	1562	—	3.8
635	1.027	1.9	22	—	4.9
603	1.028	3.3	681	1.030	2.5
59	1.029	0.9	602	1.025	2.4
198	1.023	1.8	153	1.027	5.6
45	1.028	1.8	152	1.028	1.6
K.	1.027	1.7	A.	1.022	1.7
29	1.023	2.0	793	1.026	1.4
94	1.022	0.7	796	1.028	1.7
460	1.024	1.7	787	1.026	1.7
113	1.022	1.3	593	1.023	1.9
291	1.023	5.5	177	1.023	1.6
149	1.024	1.2	253	1.027	1.5
74	1.023	2.4	790	1.024	1.9
409	1.024	1.3	2152	1.028	2.6
57	1.019	0.8			

Average of 40 medical students and laboratory workers — 1.0

\* Kindly prepared for us by Prof. H. E. T. Haultain, of the Department of Mining Engineering of this University.

On inquiry as to where the men had been working prior to coming off shift, it was found that in many instances those showing high silica values had been in the dustiest parts of the mine. The variations did not always correspond, however, to the amounts of dust to which the men had been exposed. The average of the mining group was about two and one-half times the urinary output of silica in a large group of students in Toronto.

In view of the fact that the ingestion of silica so markedly increases the output of silica in the urine, too much emphasis cannot be placed on the values found. Moreover, diet is an important factor in influencing the excretion of silica and it was found impossible to gain a knowledge of the diet of these mine workers. In order to rule out the possibility of high silica values being related to concentrated urines, specific gravity determinations were made on most of the specimens. It will be seen from Table II that the silica content of the urines is quite independent of the specific gravity.

The twenty-four hour output of silica was studied in a group of six miners on seven different occasions during periods when they were not exposed to the dust. Drs. N. R. Russell, H. H. Moore and W. D. Robson kindly cooperated in securing the specimens. Despite wide variations, the results appeared to indicate that miners away from their work and not exposed to dust continue to excrete silica in amounts

normal, healthy laboratory workers were subjected during the course of most of one day to an atmosphere containing large amounts of finely particulate silica. It was thought worth while to collect the urine during the following twenty-four hours from each of these persons for analysis. The results showed in each case an output of silica which was definitely higher than normal (as judged by the excretion of silica one week later), the second and third case being considerably higher than the first.

It seemed worth while to attempt to determine whether the amounts of silica dissolved and excreted in the urine of men with silica deposits in their lungs could be influenced experimentally. If silica in the lung is dissolved by the action of the mildly alkaline tissue fluid, it might be possible to accelerate the rate of solution by increasing the alkali reserve of the blood plasma. Although there would be no appreciable change in the actual pH of the blood, the extra available alkali bicarbonate might bring about the solution of more silica. The results of the administration of alkali to silicotic patients, and to dogs who had received intratracheal administration of powdered quartz, were, however, indecisive. Although some increases were observed, the results were too erratic for any conclusion to be drawn. It had been hoped to follow the excretion of silica on twenty-four hour samples, but it was found impossible to do so. No significant increases were observed in the percentages of silica in the urine samples, but since the total daily output was not known, it cannot be said whether or not there was an increased excretion of silica.

It has been suggested that some phagocytized particles may find their way from the alveoli up the bronchial tree into the trachea and may be either swallowed or expectorated in the sputum. Irwin<sup>5</sup> has brought forward evidence in this connection by the demonstration that cells of the reticulo-endothelial system which have ingested particles of thorium dioxide migrate through the lung until they are found in the upper respiratory tract and finally in the trachea. In the sputa of persons exposed to siliceous dust, then, it might be expected that considerable amounts of silica would occur. No sputa from such cases have been available, but several samples were obtained for us by Dr. C. B. Ross from sanitarium patients in Graven-

TABLE III.

URINARY SILICA OF NORMAL PERSONS EXPOSED TO QUARTZ DUST.

	Mg. SiO <sub>2</sub> per 100 c.c.	c.c. of urine	24 hr. output of SiO <sub>2</sub> (mg.)
F. ....	1.70	1,600	27
H. ....	3.20	2,010	64
K. ....	3.23	1,580	51
Twenty-four hour specimens taken in the same containers 1 week after exposure.			
F. ....	0.97	1,660	16
H. ....	0.75	2,000	15
K. ....	0.40	1,750	7

well above that of the non-mining population. The normal daily excretion of silica for people without exposure to dust is about 10 to 15 mg., and the output among these men ranged from normal to nearly 50 mg. for the twenty-four hour periods.

During the course of some experiments in this laboratory with finely ground quartz dust, three



hurst. In most of these cases, both silicotic and control, there was destructive tuberculosis, and, as might be expected, those patients with silica deposits in their lungs excreted siliceous material in the sputa. Since the sputa were all extremely viscous and difficult to handle, the analyses were carried out on samples of the sputum transferred directly from the Bakelite test tubes to platinum crucibles, and weighed without drying. The results are complicated, therefore, by the presence of varying amounts of moisture in the specimens. Among the silicotic group the case RB gave definitely the highest value found.\* (See Table IV). RB

TABLE IV.  
THE SILICA CONTENT OF SPUTUM

Non-Silicotic Group			Silicotic Group		
Mg. SiO <sub>2</sub> per 100 g.			Mg. SiO <sub>2</sub> per 100 g.		
Case	sputum (wet weight)		Case	sputum (wet weight)	
	Mar. 24 (1933)	Apr. 28		Mar. 24	Apr. 28
Br.	0.17	—	RB	1.49	1.97
Du.	0.55	—	Lu.	0.48	—
Do.	—	0.21	Le.	—	0.50
Ki.	0.80	—	Oi.	0.41	—
La.	0.14	—	Su.	0.24	—
MG	—	0.33	So.	—	1.25
Pr.	—	0.22	Tr.	—	0.74
Sm.	0.23	—	Yu.	—	0.45
			Coal miner		
			(Scotland)		4.03

had "... extensive silicosis coupled with a destructive tuberculosis and the sort of sputum one would expect with such a lesion." The lower values were associated with the presence of less destructive tuberculous lesions in the lungs. Su, for instance, "... had a prolonged exposure to mine dust. ... his general condition is good; the lung changes are essentially fibrotic with no evidence of exudative or destructive changes. What little sputum he has is probably catarrhal with post-nasal elements."

"As regards the controls, I note that Ki's estimation is at least twice as high as the average of all cases, excluding RB's. In checking Ki's history I find that he is a painter and decorator by trade. He has had to handle considerable mica-finished wall paper, and in the handling and brushing of it he has been troubled with dust. He has followed this trade for years.

\* Since these samples were analyzed, Dr. W. P. Warner has supplied us with the sputum of a former coal miner who had an exposure over several years to carbon and silica dust. His sputum was dark grey in colour, indicating the presence of carbon, and contained a large amount of silica (4.03 mg. per cent).

He is suffering from a moderately advanced tuberculosis, the lesion being moderately exudative and destructive. Du, whose estimation was 0.55, gives a history of having worked for more than two years in Scotch coal mines."\*

The silica content of the blood was determined in several cases. The blood was collected by Dr. Ross at the sanitarium, and was analyzed by the method for total silica in blood as described elsewhere.<sup>1</sup> All the patients examined were tuberculous, some of whom had a history of exposure to silica.

TABLE V.  
MG. OF SILICA PER 100 C.C. OF BLOOD.

Non-silicotic		Silicotic	
Br.	0.92	Rb	0.96
Du.	0.80	Br.	0.54
Ki.	0.86	Lu.	0.66
La.	0.68	Su.	0.95
Sm.	0.76	Oi.	0.67

There appears to be no significant difference between the level in the blood of the non-silicotics and of the silicotics. This is in agreement with the findings for animals which were injected with silica and in which no appreciable increase of the blood silica was found, despite the fact that the urinary silica rose to high levels. Because of the low kidney threshold for silica, a silicotic person dissolving any significant amount from his lungs would probably excrete it almost immediately in the urine.

#### SUMMARY

Silica in small amounts appears to be a natural constituent of all animal tissue.

Silica which reaches the blood stream, either by absorption from the gut or by solution in the lung, is rapidly excreted in the urine. Soluble silica injected into the blood is quickly eliminated in the urine. There appears to be a low kidney threshold for silica.

The urinary excretion of silica is at a higher level in persons exposed to silica dust than in normal persons.

Attempts to influence the absorption of silica from the lungs by administration of alkali gave inconclusive results.

The elimination of silica by way of the sputum from patients having deposits of silica in their lungs appears to be higher than in those having no history of exposure to dust.

\* Communications from Dr. Ross.

Only small amounts of silica are present in the blood. No significant differences were found between its level in the blood of normal and silicotic persons.

Our thanks are due to Dr. F. G. Banting for suggesting this research to us, and for his help and advice during the course of the experiments.

#### THE COLORIMETRIC DETERMINATION OF SILICA IN URINE

The colorimetric procedure for the determination of silica in the urine consists in the production of a silicomolybdic acid complex which is reduced to give a blue colour, the depth of colour being proportional to the amount of silica present. For the determination a phosphate-free filtrate must be obtained. This may be accomplished by the use of  $\text{NH}_4\text{OH}$  and  $\text{CaCl}_2$  (King and Stantial, 1933). In this procedure the precipitation of phosphate is carried out at an alkaline reaction, and as a result glass vessels cannot be used. To avoid the alkaline precipitation the method described by Jacobs (1929) for the precipitation of phosphate, iron and protein from blood has been adapted for urine analysis. As the mixture is at no time alkaline, the whole procedure may be carried out in glass. The method described removes phosphates as ferric phosphate, excess iron as basic ferric acetate, any proteins, fat and debris, and a portion of the urinary pigment. The amount of urine used will depend on the silica content. One c.c. of the urine of rabbits or other herbivora which have a high output of silica, and 5 c.c. of human urine are usually appropriate amounts to give a convenient depth of blue colour in the test solutions.

**Reagents.**—All chemicals must be silica-free and blanks should be run frequently to ascertain that no contamination of the reagents has occurred.

#### $\text{N H}_2\text{SO}_4$ .

Twenty-seven decimal eight c.c. of concentrated sulphuric acid made to 1 litre with water.

#### Ferric chloride solution.

Ten per cent ferric chloride ( $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ ) dissolved in 0.2 N HCl. Twenty c.c. of this stock solution are diluted to 200 c.c. for use in analysis.

#### N NaOH.

To obtain a silica-free sodium hydroxide solution, 2.3 g. of metallic sodium are dropped in small pieces into water in a nickel crucible packed in ice. The solution is made up to 100 c.c. and stored in a wax bottle.

#### Sodium acetate solution.

Three decimal seven five g. of crystalline sodium acetate ( $\text{NaC}_2\text{H}_3\text{O}_2 \cdot 3\text{H}_2\text{O}$ ) are dissolved in water, 7 c.c. N NaOH added, and the solution made to 250 c.c. This solution is kept in a wax bottle.

Pipettes should be brought into these alkaline solutions for only the briefest time.

#### Molybdate sulphuric reagent.

Ten g. ammonium molybdate are dissolved in 200 c.c. of N  $\text{H}_2\text{SO}_4$  with shaking.

#### Aminonaphtholsulphonic acid solution.

Thirty g. sodium bisulphite, 6 g. sodium sulphite, 0.5 g. 1, 2, 4-aminonaphtholsulphonic acid, are dissolved and made up to 250 c.c. The main part of this solution is preserved in the ice-box and a small amount kept in a brown glass bottle on the bench for use.

#### Standard silica solution.

Crystals of sodium silicate ( $\text{Na}_2\text{SiO}_3 \cdot 9\text{H}_2\text{O}$ ) may be used in the preparation of the standard solution, but owing to variation of the water content it requires very careful standardization against picric acid (King and Lucas, 1928) and consequent adjustment each time it is made. It has been found more satisfactory to use pure fused lumps of anhydrous potassium silicate ( $\text{K}_2\text{SiO}_3$ ). As this substance is very hygroscopic, the sample should be ground in a mortar as quickly as possible on a dry day and stored in a weighing bottle in a dessicator. Twenty-five decimal seven mg. of this

dry salt dissolved in water and made up to 1 litre gives a solution 10 c.c. of which contains 0.1 mg.  $\text{SiO}_2$ . This solution will keep for 3 or 4 weeks, but as routine practice a fresh supply is made each week. In weighing, a small amount is transferred to a covered weighing bottle with as little exposure to air as possible, weighed, and made up to the required volume. If the  $\text{K}_2\text{SiO}_3$  has been kept dry, and the weighing carried out carefully and quickly, no further adjustment will be necessary.

#### METHOD

One to 5 c.c. of the urine to be tested is placed in a 250 c.c. Erlenmeyer flask, and made just acid to methyl orange with acetic acid. Equal quantities of the ferric chloride and sodium acetate reagents are added and water to 25 c.c. The solution is brought quickly to the boil, with constant shaking, the precipitate allowed to coagulate for a minute and then filtered while still hot through a No. 32 Whatman filter paper. The quantity of precipitating agents added must be determined by trial, as different urines require different amounts. Five c.c. of normal human urine is usually cleared of phosphate by 5 c.c. of each of the reagents, while 10 c.c. of the reagents is sometimes not sufficient for 2 c.c. of dog urine. The filtrate should be clear and practically colourless. If the urinary pigment is not removed 0.5 g. of finely powdered charcoal or active carbon (silica-free) is added and a blank determination carried through. If any colour is obtained on the addition of the reagents the value is subtracted from the test to give the true silica content of the urine.

One c.c. of the filtrate is tested for phosphate in a small test tube by the addition of 2 c.c. N  $\text{H}_2\text{SO}_4$ , 4 drops ammonium molybdate in N  $\text{H}_2\text{SO}_4$  and 2 drops of the aminonaphtholsulphonic reagent. The development of any blue colour indicates the presence of phosphate and the precipitation must be repeated, using more of the iron and acetate reagents.

A second 1 c.c. portion is tested for iron by adding 2 or 3 drops of a potassium ferrocyanide solution and a drop of dilute acetic acid. When iron is present in the filtrate as shown by the formation of a green colour, the development of the blue colour in the silica determination will be retarded. A slight alteration of the pH of the urine will usually result in the filtrate being iron-free.

If the filtrate is iron- and phosphate-free the silica is determined colorimetrically as follows. An aliquot portion of the filtrate (e.g., 15 c.c.) and 2, 5 and 10 c.c. of silicate standard (0.02, 0.05 and 0.1 mg.  $\text{SiO}_2$ ) are pipetted into 25 c.c. flasks and the volumes made to about 20 c.c. Two c.c. of the 5 per cent ammonium molybdate in N  $\text{H}_2\text{SO}_4$  are added, and the solutions allowed to stand 5 minutes. One-half c.c. of aminonaphtholsulphonic acid is then added, the volumes made up to 25 c.c. and the solutions mixed. The blue colours are compared after 5 minutes in a Duboseq colorimeter.

#### Calculation:

Reading of Standard	conc. of Standard	25
	X	X
Reading of Test		c.c. filtrate used
	100	mg. $\text{SiO}_2$ per
X	c.c. urine used	100 c.c. urine

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PARATHYROID DISTURBANCES FOLLOWING THYROIDECTOMY:  
WITH REPORT OF A CASE\*

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ETIOLOGICALLY, tetany may be divided into five types: those

1. Due to vitamin deficiency; infantile tetany or spasmophilia.

2. Due to alkalosis; (a) gastric, (b) hyperpnœic.

3. Due to relative parathyroid deficiency; (a) menstruation, (b) pregnancy, (c) parturition, (d) lactation, (e) infections.

4. Due to acute infectious diseases and intoxications. Here the infection or intoxication seems to be the precipitating factor. It may act by paralyzing the parathyroid glands, thus producing a deficiency of hormone.

5. Due to destruction or disturbance of the blood supply of the parathyroid glands following thyroidectomy; post-thyroidectomy tetany.

Infantile tetany, or spasmophilia, is the most common form of tetany and occurs in the so-called tetany months of March and April. It is caused chiefly by insufficient exposure to sunlight and vitamin D deficiency, and thus is frequently found associated with rickets. With this etiology it is quite possible for spasmophilia to occur in adults as well as in infants. In fact, in a critical analysis of the literature Leopold and Jonas<sup>1</sup> re-classify, as infantile tetany, 528 cases of occupational idiopathic tetany in males (223 cobblers and 117 tailors) collected by von Fränkl-Hochwart, and quoted by Falta and Meyers.<sup>2</sup>

In tetany due to alkalosis, that of gastric origin may be found in many gastro-intestinal affections, as typhoid fever, appendicitis, pyloric obstruction, etc. Here the parathyroids are normal, but an alkalosis is produced by the loss of hydrochloric acid from the vomiting. It does not require prolonged emesis, but may occur after vomiting only two or three times.

Hyperpnœic tetany is produced by excessive pulmonary ventilation, with the resulting loss of carbon dioxide and the production of alkalosis.

Relative parathyroid deficiency, resulting in the clinical signs of tetany, may appear when there is an increased demand on the parathyroid glands to which they are unable to respond. This extra demand may occur as the result of menstruation, pregnancy, parturition, lactation or infection. Von Fränkl-Hochwart reported 53 cases of this type, which were quoted by David Marine<sup>3</sup>—28 cases occurring late in pregnancy, 19 shortly after delivery, and 29 during lactation.

Tetany may be produced by the toxæmia of dysentery and cholera, or intoxication from lead, ergot, phosphorus, morphine and uræmia. In the first two conditions, the associated diarrhœa, with increased calcium excretion, is a factor in precipitating tetany. Other unknown toxins are possibly the cause of those few cases of tetany reported in the literature as idiopathic tetany. Liu<sup>4</sup> reported a single case in a Chinese male, aged 46 years, and Leopold and Jonas<sup>1</sup> one case in a white male of 38 years. There is a marked similarity in these two cases.

Post-operative tetany follows accidental removal of, injury to, or interference with the circulation of the parathyroid glands. This usually occurs during resection of the thyroid gland, and may be a very transitory condition, manifesting itself a day or two following the operation with mild symptoms which are easily controlled. In these cases, moderate stiffness of the hands may be the only complaint. Small doses of calcium and parathormone alleviate the symptoms, which do not recur. Obviously these patients suffer only a very temporary parathyroid dysfunction. In other cases where most of the parathyroid tissue has been removed or destroyed by crushing with forceps or ligatures, chronic post-operative tetany results. Rarely it happens that two or three weeks after operation a patient develops a marked induration of the soft tissue of the neck with subsequent fibrosis. In these cases the fibrosis causes great damage to the parathyroids, and even to the remaining

\* Read before the American Association for the Study of Goitre at Memphis, Tennessee, May, 1933.



thyroid tissue. I wish to report a case of post-operative tetany which we have followed for nearly seven years. This patient had a mild, transitory tetany appearing on the second day after operation and disappearing on the fifth day. Two weeks later induration of the neck occurred, and severe tetany appeared in the third week after operation.

#### CASE REPORT

M.H., a female, white, married, aged 36 years, first came under our observation in July, 1926. In three years she had lost 56 pounds in weight. One and a half years before we saw her she went through a pregnancy, during which she was in very poor health. In January, 1926, she first observed a swelling in her neck, and in February exophthalmos was noticed. She complained of nervousness, restlessness, insomnia, tremor, and leg weakness. This last symptom was most disabling, as she could not get up one step without pulling herself up with her hands. Her voice had been husky for three months. Her skin was flushed, and she had heat intolerance.

On examination, she weighed 106 pounds, was emaciated, and presented marked exophthalmos, tremor and flushing. The thyroid was moderately enlarged, diffuse, smooth and very firm. The tonsils were definitely infected. The pulse rate was regular, at 110 per minute. The blood pressure was 164, systolic, and 50, diastolic. Laboratory studies were essentially negative, except the basal metabolic rate, which was plus 91 per cent. She was admitted to hospital on August 11, 1926, and responded well to a régime of rest and Lugol's solution. The pulse rate dropped to 80 per minute, but nervousness and restlessness were not well controlled. At this time we were doing a two-stage operation on severe cases. On August 27th a left lobectomy was done under gas-oxygen anaesthesia. The left lobe was about five times its normal size; it extended very high in the neck and well around behind the trachea. The gland was firm, friable and diffusely hyperplastic. Only a mild reaction followed the operation, and the patient was sent home for two months. During this period she gained 40 pounds in weight, and her general condition was much improved.

On November 13, 1926, a right lobectomy was done. This lobe extended high in the neck, behind the trachea, and well down behind the sternum. The character of this lobe was the same as the left. The pathological report stated that the tissue on section was alveolar in appearance and showed the presence of no adenoma. The microscopic diagnosis was hyperplastic goitre of the exophthalmic type.

On the second morning after operation the patient complained of some stiffness of the hands, which was controlled and disappeared in three days on treatment consisting of calcium lactate, grains ten, with desiccated parathyroid gland, grains one-tenth, three times daily. On the fifth day after operation the patient's condition was good and she was discharged from hospital.

Towards the end of the second week after operation a firm, brawny induration of all the soft tissues of the neck developed. There had been no drainage from the wound previously, nor did any develop later. Signs of tetany again appeared, and calcium lactate and desiccated parathyroid gland were administered, supplemented by calcium chloride intravenously. This seemed to control the tetany for a few days, but the induration of the neck became more marked and the tetany harder to control.

On December 12th the patient had a generalized convulsion, and the next day, just one month after operation, she was re-admitted to hospital. She was spastic, drowsy, and recognized no one. On December 20th she had a generalized convulsion lasting seven minutes. Her serum calcium on that date was 8.71 mg. per 100 c.c. We started diathermy treatment on her neck, which by this time was extremely hard. On December 22nd her serum calcium was 9.4, yet she was very confused and restless. On the same date we discontinued desiccated parathyroid gland and substituted parathormone (Collip). On December 24th, with a serum calcium of 7.84, she had a good day and recognized her family for the first time since admission to hospital. (Fig. 1).

A constant dose of twenty grains of calcium lactate, given three times daily, was maintained throughout treatment in hospital. Small doses of desiccated thyroid gland were administered for one week, from December 27th. The dosage of parathormone was varied greatly in order to study its effect on the serum calcium. It soon became apparent that the serum calcium could be controlled by the amount of parathormone administered, but maintaining the serum calcium within normal limits did not necessarily control the uncomfortable symptoms of tetany. Unfortunately, during the acute phase we were not in a position to make blood phosphorus estimations, but at the time of reporting the blood phosphorus was 4.75 milligrams per cent.

From January 12 to 29, 1927, the serum calcium was maintained at between 9 and 10 milligrams, and the induration in the neck was subsiding. On the latter date the patient was discharged from hospital. Calcium lactate was then replaced by calcium chloride, twenty-four grains in capsule three times daily, and for two months ten units of parathormone were administered every second day. In April a mild hypothyroidism was apparent, and the administration of five grains daily of desiccated thyroid gland was begun, and the parathormone replaced by desiccated parathyroid gland.

She still complained of stiffness of her jaws and hands, and clumsiness. She frequently fell for no apparent reason. On two occasions when she fell off her chair her serum calcium was estimated, and found to be 10.2 mg. on the first occasion and 7.44 on the second. This latter attack occurred during menstruation (Fig. 2).

In March, 1927, an acute tonsillitis developed, and the serum calcium dropped rapidly from 10.46 to 7.06 mg. per cent (Fig. 2). In April her tonsils were removed under local anaesthesia. Thereafter 24 gr. of calcium chloride daily and one-tenth gr. of desiccated parathyroid gland every second day maintained her serum calcium at between 9 and 10 mg. Her basal metabolic rate at that time was minus 6 per cent (Fig. 2).

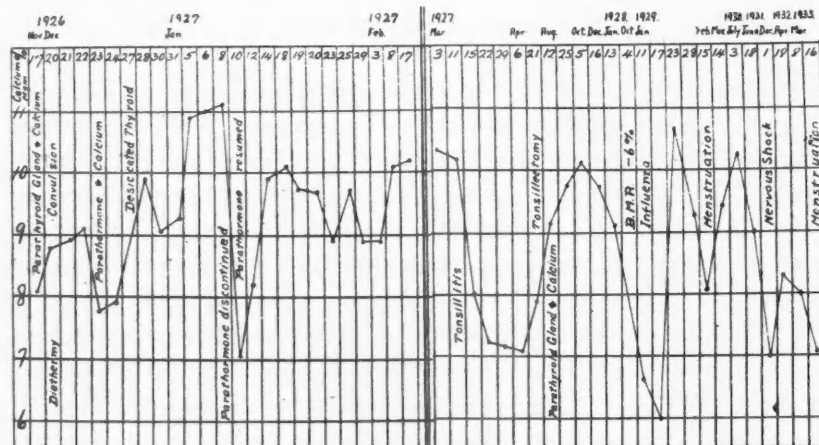


FIG. 1

FIG. 2

On January 4, 1929, she developed a mild influenza, but got up daily to attend to household duties. Insomnia, restlessness and spasticity developed. On January 11th the serum calcium was 6.64, and on the 17th 6 mg. per cent, but on the latter date the patient stated that she felt fine and was out for a walk. The calcium was increased and parathormone again used. On January 23rd the serum calcium had increased to 10.6 mg. per cent (Fig. 2).

Menstruation always aggravated the patient's subjective symptoms, and resulted in a sharp fall in serum calcium (Fig. 2).

In 1931 the patient had a severe shock in the sudden and unexpected death of a kind friend and benefactor. This resulted in a complete mental upset lasting about one week. She was excitable, talkative, restless and sleepless, and her serum calcium dropped to 7 mg. per cent. In the interval between these various exacerbations, small doses of desiccated parathyroid gland, calcium chloride, and thyroid gland have kept the patient fairly comfortable, and able to do a certain amount of housework. However she is easily fatigued. This is most noticeable in the arms, which tire very easily.

#### CONCLUSIONS

1. Post-operative tetany may appear late and be caused by induration and fibrosis of the soft tissues surrounding the parathyroid glands. In such cases it may be very severe, but can be controlled, with the expectation that after a few months the parathyroid glands will regain at least part of their function.

2. During acute infections, such as tonsillitis and influenza, there is an increased demand on the parathyroid glands. The damaged glands in

this case could not meet these demands, and the serum calcium fell, and symptoms of tetany manifested themselves.

3. Menstruation also increases the demand on the parathyroid glands, and in this patient resulted in exacerbation of her symptoms and a fall in serum calcium.

4. Nervous shock influences calcium metabolism, and in this case of chronic tetany produced a marked exacerbation of symptoms and a fall in serum calcium.

5. The level of the serum calcium can be controlled by administering parathormone and calcium, but the severity of the patient's symptoms is not wholly dependent upon the level of the serum calcium. In December, 1926, this patient had a generalized convulsion when her serum calcium was 8.86 mg. per cent. In January, 1929, she stated she felt fine and was out for a walk when her serum calcium was only 6 mg. per cent.

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### THE INJECTION TREATMENT OF HÆMORRHOIDS

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**HÆMORRHOIDS** are a varicose and hypertrophied condition of the anal canal and the lower part of the rectum. They are classified as internal and external. Internal hæmorrhoids are of the first, second and third degree; the last two are infrequently associated with external hæmorrhoids.

Briefly, the complaints are irritation, protrusion of a mass at stool, and bleeding. The diagnosis is usually made without examination, and the patient given some type of ointment. *Herein lies the unpardonable sin.* There are numerous other conditions of the rectum and the anal canal which give a similar history and are easily ruled out by careful examination. They are as follows: carcinoma of the rectum, and the anal canal, benign or malignant papilloma of the rectum, varices due to cirrhosis of the liver or

heart disease, tuberculous ulceration, luetic ulceration, paraffinoma of the rectum. Do not fail to do a complete physical examination including digital examination of the rectum, proctoscopic, if possible, assisted by a Wassermann test and a biopsy.

The complaints are infrequent bleeding at stool, spotting or profuse, itching, a bearing-down feeling, the protrusion of a mass at stool, which has to be replaced, discomfort on sitting down, and, in the case of a thrombosed external hæmorrhoid, very severe pain on walking or sitting.

Let us consider the structures comprising a hæmorrhoid. They form a tumour mass, which may be compared to a grape on a stalk. The stalk is the pedicle, which contains a small branch of the hæmorrhoidal arterial anastomosis

and a tributary of the hæmorrhoidal veins. The body of the hæmorrhoid consists of hypertrophied mucous membrane, elevated and prolapsed from the muscle of the bowel wall, beneath which are the ramifications of the hæmorrhoidal artery and vein, separated by newly developed fibrous tissue from the muscle of the bowel.

There are three primary hæmorrhoids, situated at 4, 7, and 11 o'clock. This distribution is explained on the basis that the right branch of the superior hæmorrhoidal artery divides into two terminal branches, which supply the 7 and 11 o'clock hæmorrhoids, respectively. The left branch of the superior hæmorrhoidal artery on the other hand does not subdivide, and supplies the area corresponding to the 4 o'clock hæmorrhoid. Secondary hæmorrhoids take up an intermediary position.

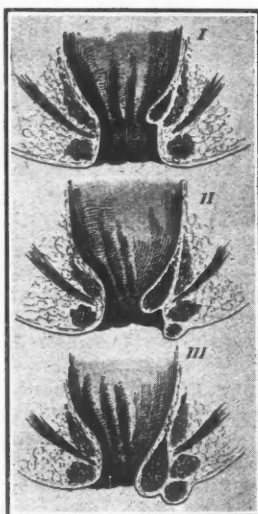


FIG. 1—Showing first, second, and third degree internal hæmorrhoids.

Hæmorrhoids of the first degree are small and are situated entirely above the mucocutaneous junction (Hilton's). The only symptom is bleeding, which is usually slight, but may be considerable. Hæmorrhoids of the second degree form a fleshy mass which is protruded on defæcation, but returns spontaneously after the act, or can be readily returned by the patient. Above the pile, the thickened vascular pedicle may be seen. The mucosa below Hilton's line is raised from the subjacent muscle, and fibrous tissue is deposited between these two layers and also superficially to the sphincter, where it forms an external pile at the anal orifice. The upper part of the pile is covered by thickened mucosa and the lower part by skin. There is a well marked furrow between the external and the internal piles. The sphincter can retain the internal pile, but not the external. The bleeding is less, but prolapse is frequent. Hæmorrhoids of the third degree have the outstanding feature of intractable prolapse, due to the size, shape and laxity of the pedicle. Bleeding is not common. If not reduced, they frequently ulcerate and become

gangrenous. Pyelo-phlebitis may develop. External hæmorrhoids are found in association with internal hæmorrhoids, or separately.

The treatment varies according to the classification. External hæmorrhoids should never be injected, otherwise severe discomfort will ensue. If thrombosed, inject with a local anæsthetic and shell out the blood clot; if not thrombosed, ligate and allow to slough, or excise and suture.

Internal hæmorrhoids are treated by numerous methods. The method used depends upon the type of hæmorrhoid, that is, whether first, second, or third degree. The cautery or diathermy may be used, but the results are poor, and the risk of hæmorrhage is great, since the pedicle is not controlled. First and second degree internal hæmorrhoids are treated by injection. Paraffin block has been used to dam back the mucous membrane, with resulting stricture of the rectum due to paraffinoma. Operations of various types are used, such as resection, followed by cautery and suture of the eschar, simple resection with ligation of the pedicle; resection of the pile-bearing area (Whitehead's operation) is used for a complete protruding ring of prolapsed hæmorrhoids. Stricture of the rectum must be guarded against, otherwise rectal dilatation will be necessary.

The principle applied to treatment of hæmorrhoids, whether carried out by injection or operation, is exactly the same. In the presence of infection treatment is only palliative until the infection clears; otherwise, pyelo-phlebitis will ensue. Treatment consists of obliteration of the branch of hæmorrhoidal artery and vein in the pedicle, and anchoring the redundant rectal mucosa and the body of the hæmorrhoid. In operation, the pedicle is clamped and ligatured, the body of the hæmorrhoid removed, and the mucosa fixed by scar to the muscle of the bowel wall. In injection, the pedicle is obliterated by contraction of the surrounding scar tissue produced by the sclerosing agent; the body of the hæmorrhoid is replaced by scar tissue, thereby diminishing its volume and fixing the mucosa again to the muscularis of the bowel, thus preventing prolapse.

There are limitations which must be borne in mind regarding the injection treatment of hæmorrhoids. If carefully considered, the results will be quite satisfactory. Only first and



second degree hæmorrhoids are suitable for treatment by injection; under no circumstances must a third degree or external hæmorrhoid be treated by injection, otherwise a thrombosed prolapsed mass is produced which is extremely painful, both on walking or sitting, relief from which is only given by surgical procedure.

Bleeding is the only discomfort in first degree hæmorrhoids. This is almost immediately stopped by injection. In the aged and infirm, to whom the risk of an anæsthetic is grave, injection will give a satisfactory relief of symptoms. From an economic point of view, the injection treatment does away with hospitalization and lends itself as an office treatment. It gives relief of symptoms, but is only considered a three-year cure, after which time further injection or operation is necessary. The great advantage is, that the patient may carry on with his daily occupation without undue discomfort.

The technique is simple, necessitating the following: an anoscope; 1 c.c. tuberculin syringe; long fine needle, gauge No. 22, 2 inches long; dressing forceps and swabs, an adequate focussing illuminating lamp; and the solution to be used, which may be any one of the three following. If 5 per cent phenol in almond oil is used a 10 c.c. glass syringe with a Morley needle, with a special Luer-lock attachment, is used. This has the advantage that the needle, due to the resistance of the oil, will not part company with the syringe, and, further, the point of the needle has a guard for depth.

1. Swinford Edward's solution (20 per cent carbolic).  
Two parts, water.  
One part, phenol.  
Two parts, glycerine.  
*Dose:* 2.5 minims produces small areas of sclerosis and does not produce ulcers or slough.
2. Five per cent phenol in almond oil.  
*Dose:* 0.5-2 c.c.; injection made slowly until Blanchard's striation sign shows (the vessels are seen as red threads crossing a white surface).
3. Quinine-urethane solution.  
Quinine hydrochloride 4 grams.  
Urea 2 "  
Water 30 c.c.  
*Dose:* 3-7 minims. The great danger is slough and ulceration, which is very painful on defæcation.

The injection treatment is carried out as follows: One seance of injections per week, extended over a period of eight weeks, is usually necessary for the obliteration of the hæmorrhoids. Two or three injections are made per

seance, starting with the pile pedicles, and then continuing into the body of the hæmorrhoid, unless there is profuse bleeding, when the first seance of injections are made into the body of the hæmorrhoid, and at the second seance the pedicle is injected.

The evening before the day of the first injection, the patient is instructed to take by mouth one oz. of castor oil, and 12 hours before coming to the office, a saline injection per rectum. This facilitates a very good examination of the rectum and anal canal with the anoscope prior to the first injection. Throughout the whole course of injections, the patient is instructed to educate his bowels to regular habits, and facilitate soft motions with Russian oil, and milk of magnesia, also to replace any prolapsed masses after stool.

An injection seance is carried out quite simply. The tuberculin syringe fitted with long fine needle is sterilized and loaded with the solution to be used, and placed in a sterile kidney basin with swabs and dressing forceps at the operator's right hand when the patient is in the knee-chest position. The patient is then placed in the knee-chest position, to allow the rectum to balloon out by atmospheric pressure as the small bowel recedes. The anoscope, sterile but warm, is introduced into the rectum, and a strong focussing light is cast into the anoscope over the operator's right shoulder. The anoscope is very gradually and slowly withdrawn, so as to expose the summit of the pile pedicles. The needle is then introduced into the submucosa at the upper end of the pile pedicle, the plunger of syringe withdrawn for a short distance to make sure that the needle is not in the lumen of a vessel, and then the solution is injected. If Swinford Edward's solution is used, 3.5 minims are injected. The pedicle becomes swollen and œdematous, and after a lapse of half a minute the needle is withdrawn. Three pedicles may be injected per seance. If 5 per cent phenol in almond oil is used, 0.5-2 c.c. are injected into the submucosa, until Blanchard's striation sign appears. At the second seance the body of the hæmorrhoid is injected, and so on until sclerosis is complete. If a thrombosed area should prolapse, remove it under local anæsthesia.

I have had patients refuse operation after three years' interval in preference to another course of injections, which lasted only for four seances.

In conclusion, the injection treatment of hæmorrhoids is considered an office procedure, painless, does not necessitate loss of time from business on the part of the patient, nor does it incapacitate him in any way. On the contrary, symptoms are relieved, bleeding stops, prolapse is overcome, and the dragging feeling is no more. Injection is extremely useful for the relief of symptoms in the aged who are unable to stand an anæsthetic. It must be borne in mind that at the most it is a three-year cure, and can only be used for hæmorrhoids of the first and second degree, and under no consideration must it be used for external hæmorrhoids.

My own preference is for the 20 per cent carbolic in glycerine, but I frequently use the 5 per cent phenol solution. The 20 per cent solution produces smaller sclerotic nodules, and therefore does not give the rectum the feeling of the presence of a small mass of fæces which must be extruded. Care must be taken against using too large a quantity of sclerosing solution, otherwise stricture of the anal canal may ensue, and, above all, do not use quinine and urethane solution for injection purposes, otherwise you may produce injection ulcers which are extremely painful each time the bowels move.

### MACULAR ABERRATION AND THE REVERSAL OF THE MACULAR CURVATURE

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IT is somewhat surprising that the aberration due to the inequalities of the retina at the macula has attracted practically no attention; the more so as conditions about the fovea plainly indicate that aberration must exist. To some extent, doubtless, this is because the effects of the aberration have to be demonstrated to be appreciated, but it is also largely due to the fact that Von Helmholtz attributed Gauss' phenomenon of the dots to the general curvature of the eye-ball. He constructed his hyperbolic damier or checker-board to demonstrate this curvature, but neither in this nor in Tscherning's model eye, which apparently proves the correctness of the construction, is there any recognition of macular aberration.

The main reason, however, for this want of recognition is that the retinal images of lines to which attention is directed pass through the fovea (at A, Fig. 1) and in them the aberration, being congruent with the line, is not perceived. Lines which are imaged on the macula at about B are seen as concave toward the line of fixation, and lines which pass through C should show a reverse curve, but this the writer has been unable to demonstrate, this part of the retina being probably not supplied by the macular bundle.

Gauss' effect is usually demonstrated by placing two dots on paper about two inches apart, and trying to place a third in line and midway between them, while looking at a

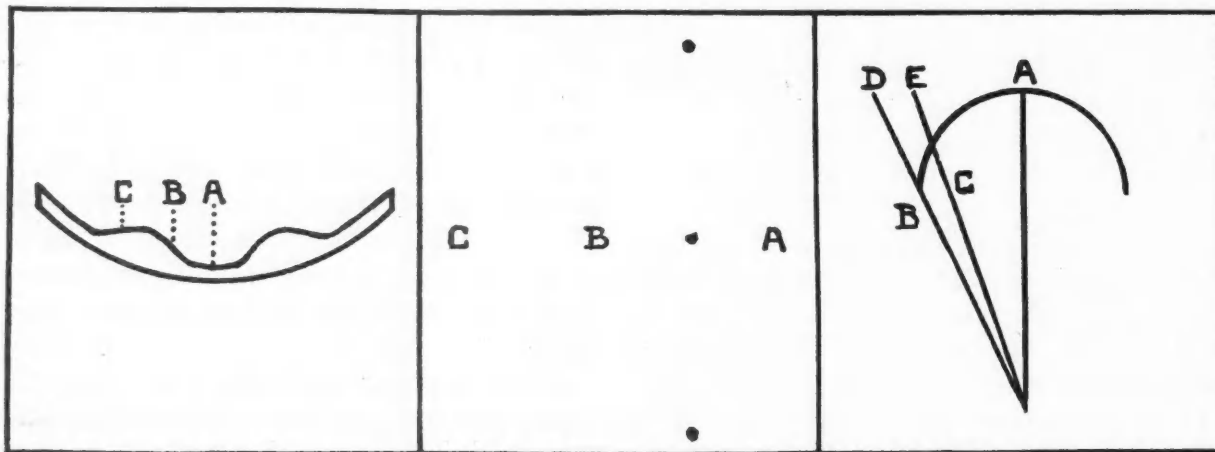


FIG. 1

FIG. 2

FIG. 3

point about  $3^\circ$  to one side of the line between the dots. The third dot is always placed out of line with the other two. A more instructive demonstration may be given by placing three dots in line (Fig. 2). If the point A be looked at the middle dot will appear to be displaced toward B; if the axis of vision be swung to B the dot will seem to move toward A while the end dots are stationary. If now the point C be looked at the centre dot will be in line with the others, showing that the effect is central and not peripheral. As the displacement is similar in all positions of the card in a given plane, it is peri-foveal, although, owing to the shape of the macula, the deviation in a line should be longer in a horizontal than in a vertical one. Macular curvature can be appreciated when the eye moves through an angle of half a degree from a line; if the motion be horizontal the curvature disappears at  $6^\circ$ , if vertical at  $5^\circ$ , so that the macula subtends an angle of  $12^\circ$  in the former and of  $10^\circ$  in the latter direction.

An interesting question arises when one considers the reversal of curvature which Helmholtz demonstrated, although he gave no history of the observation. A usual way of showing Gauss' effect is to look at the middle of the long axis of an oblong card about four inches wide. As is well known, the card seems to be widest at the middle and to taper to narrower ends, the sides being concave toward the line of fixation. If now, the card be curved into a semi-cylinder, parallel to its long axis, and looked at as before, it will seem to be narrowest at the middle and wider at the ends, the sides being convex toward the fixation point. Helmholtz seemed to consider this reversal a property of circles of his visual globe which parallel the great circle through the fixation point. As, however, his illustration shows an ordinary macular curve and not a reversed one, and, as it can be shown that light in such a plane would cause a macular curve, the explanation seems to be beside the mark. It is claimed, too, that the angles at the ends of the card appear to be greater than those at the centre, but as this would also apply to the unbent card, it cannot be the cause of reversal. I am inclined to think that this reversal cannot be accounted for in terms of ordinary physical law, and that we shall have to fall back for explanation on relativity and contrast, convincing examples of which are given by J. S.

Haldane<sup>1</sup> in his very instructive demonstration on colour-vision. Relativity in perception was recognized long before Einstein popularized the principle in his attempts to explain errors of observation in cosmic physics. We know for instance that the image on the retina of print held at six inches from the eye is twice the size of that of the same print when held at twelve inches from the eye, but it does not seem to be so. We do not judge the size of print from the retinal image alone, but also from distance, accommodation, convergence and other factors. In the old experiment of placing one hand in cold water, the other in hot, and transferring both to water of medium temperature, we get impressions that the same water is both hot and cold, an obvious contradiction. Relatively, however, both interpretations are correct. There seems to be a tendency not only for established conditions to be accepted as normal but for sudden changes in these conditions and for familiar objects perceived under unusual aspects to be misinterpreted. This tendency seems to afford the only reasonable explanation of the reversal under discussion. The writer has constructed figures seeking to harmonize the observations that both when the point of fixation is short of and when beyond the plane of observation reversal is obtained. If A, Fig. 3, the mid-point of a bent card, be looked at, while attention is directed to B, a point on the edge of the card, seen in section, B will appear to be displaced to C. There seems to be a tendency for B to be projected to the plane of A, as at D. We recognize, however, that B cannot be so far from the line of fixation as D, but the resulting correction is made proportionate to AE and not to AD. Similar construction will give comparable results when the plane of observation is between the eye and that of the fixation point, but neither affords any indication why perception of the macular curve disappears when attention is directed to some plane other than that of the fixation point. It is as if the late Mr. Maddox' foreign and home offices, if I may use the happy metaphor which he applied to the voluntary and involuntary actions of the eye muscles, had received conflicting intelligence, and headquarters consequently had made an error in judgment. It is a moot question, too, whether squint, usually attributed to fault in muscular power, is not due to dis-



turbance in the normal relations of innervation.

Contrast of the various curves which may be observed is instructive, and may be made as follows. If one faces a long vertical, as the side of a door-frame, from a distance of about ten feet and turns the head well to the right the whole line will seem to be curved to the left, owing to the obliquity of the rays and curvature of the fundus. If now, without moving the head, a point  $3^\circ$  to the left of the middle of the line be looked at macular curvature to the right, involving the middle of the line for a length which is subtended by an angle of about  $12^\circ$ , will be seen. Lastly, if, without moving head or eyes, fixation be prolonged to infinity, the macular curve will appear to be reversed, the radius of the reversed curve being distinctly shorter than that of the first and apparently than that of the macular curve also. As the same results are obtained when one eye only is used, any effect of the extrinsic muscles of the auxiliary eye is excluded.

#### SUMMARY

1. Gauss' phenomenon and allied effects have been shown to be due to macular aberration, the deviation being limited to a length of line which is subtended by an angle of about  $12^\circ$ .

2. Curvature of lines passing beyond the macula, as at C, Fig. 1, is not seen. It is suggested that this part of the retina is not supplied by the macular bundle, which alone seems to subserve accurate definition.

3. A figure showing the relation of points in the reversed curve is given. This figure is constructed from the conclusion backward, and the interpretation on which it is based is hypothetical, although it is in complete agreement with the observed conditions. No indication, except a disturbance of relativity, is given as to why a reversal of curve should occur and why the macular curve should disappear when the attention is diverted from the plane of the point of fixation.

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### CHRONIC ARTHRITIS TREATED BY CROWE'S VACCINE\*

BY J. A. NUTTER, M.D. AND E. R. WATSON, M.D.

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THE writers present their experiences at the Orthopædic Department of the Montreal General Hospital with 137 cases of chronic arthritis. All the cases reported have had at least two months' vaccine treatment, with five to twelve months' subsequent observation. The writers are acquainted with the conventional classification of chronic arthritis, in which rheumatoid, proliferative, or infective arthritis with few bone changes is distinguished from degenerative arthritis, or osteoarthritis, with many bone changes. It is well known that these types often overlap and are indistinguishable one from another. As both types, in our experience, react favourably to Crowe's vaccine no attempt has been made to differentiate one from another in the reported cases. After the age of 50, however, cases of chronic arthritis are apt to be of the osteoarthritic type. The number of such cases can

be seen in our statistics. The experience we have had in treating these cases has led us to the belief that all cases of chronic arthritis are due to infection. It is of course recognized that endocrine disturbance, especially at the menopause, predisposes to arthritis. Anæmia also is associated with arthritis in a great percentage of cases, but it is our belief that infection is probably at the bottom both of the arthritis and of the anæmia. Our cases do not include the arthritis due to gout, tuberculosis, syphilis, gonorrhœa or acute rheumatic fever.

Dr. Warren Crowe, of the Charterhouse Rheumatism Clinic, London, has been working on the vaccine treatment of chronic arthritis for over twenty years. He is the author of numerous publications on the subject. As his technique differs somewhat from that used by others we have followed as closely as possible his "Handbook of the Vaccine Treatment of Chronic Rheumatism" (Oxford University Press).

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It is, perhaps, unnecessary to point out what a crippling disease chronic arthritis is. In Great Britain, where figures are available, it has been found responsible for an appalling number of days off from work, in comparison with other diseases. Those who see many cases of chronic arthritis are often cheered by the spectacular relief from pain following the removal of some obvious focus of infection, as the tonsils or teeth, etc. On the other hand, it frequently happens that the patient, even with all possible foci removed, shows no improvement or becomes worse. Such a patient is then a most difficult problem. If infection is at fault, we cannot find or reach it. What is left to be done? Vaccine in such cases offers at least a new form of treatment which has in many cases been successful in rendering these patients symptom-free.

Vaccine treatment was begun at the Orthopædic Department of the Montreal General Hospital in September, 1932. The clinic at that time was crowded with arthritic patients, still disabled but freed from foci of infection as far as possible. This was the class to which at first vaccine was given almost exclusively with encouraging results. As the months went on we experimented with other arthritic patients still possessing obviously diseased teeth and tonsils, etc. Vaccine was given, as Crowe has recommended, to such until the appropriate dose was established. By this is meant the dose that would give several days' freedom from pain, without a headache, drowsiness, etc. Some time later, teeth and tonsils, if infected, were removed, and we found to our delight that the previous dose then good for two to three days' freedom from pain now gradually gave relief for longer periods of time and led often to a symptom-free condition. Cases in which vaccine was begun immediately after removal of foci of infection gave us more difficulty than the foregoing. Finding the proper dosage is interfered with by the post-operative exacerbation.

We have also used the vaccine to help in establishing a diagnosis. In three cases of stenosing teno-vaginitis of the thumb extensors (which, of course, is not due to infection) the vaccine did not act. It might have been so much water, whether given in large or small doses. In another case of this same disability, in conjunction with definite arthritis of the hip,

the latter was rendered symptom-free, while the thumb disability was not helped in the least. The wrist was operated on, the diagnosis confirmed, and a cure resulted.

In cases of backache following trauma a superimposed condition of arthritis was suspected. In several of these patients vaccine had no effect whatever, which was taken by us to mean that no arthritis existed. Mechanical treatment (strapping, followed by a brace) as a rule relieved these patients. Fat-fringes in the knee and the disability due to flat foot, with its accompanying pain in the internal lateral ligament, do not of course yield to vaccine, being of mechanical origin. Removal of fat-fringes by operation has been followed by relief from pain.

To sum up our experience along these lines, it may be said that if vaccine does not yield any definite improvement one should suspect some other condition, usually a mechanical one, as being at fault. This is particularly true when dealing with a patient who reacts favourably to vaccine save in some one area, such as the foot or knee. The foot or knee is very likely to reveal some mechanical weakness which will yield readily to mechanical treatment, but not, of course, to vaccine.

#### SOME COMPLICATIONS WITH THE USE OF VACCINE

Headache, if caused by the vaccine, is a very valuable symptom as indicating a general reaction, with consequent reduction of the dosage to 1/10th. Headache due to eye conditions gave us much trouble, for it was often misinterpreted as being due to the vaccine, and in consequence the dose was reduced too much. Patients who admit frequent headaches are now asked to have their eyes, etc., examined before beginning vaccine treatment. If the headache can be eliminated by glasses, etc., the proper dose can be arrived at much more satisfactorily (see case N.B.). Some 6 of our cases had their vaccine treatment delayed until their vision could be corrected. The results were excellent.

An interesting feature of arthritis is the low red cell count, with no special increase in the white cells. We have had many blood counts done, and the average has been below normal, some strikingly so. One patient had 2,600,000 red cells; another had 3,100,000. When this condition was treated and the red cells had

been increased the patient got along very much better.

Dizziness caused by the vaccine is indicative of a general reaction. In some it was found to be due to hypertension. When this is known the dose should naturally not be reduced because of this symptom alone.

We have not found any way to predict an unfavourable result from vaccine treatment. In such a case we are apt to suspect an unknown focus of infection which may need an autogenous vaccine to relieve. In an isolated joint we suspect a mechanical source for the disability.

#### STATISTICS

One hundred and thirty-seven cases of chronic arthritis are reported. Of these 65, or 47.5 per cent, became symptom-free, by which is meant that their pain disappeared while under vaccine treatment and remained away for at least five months; 35 per cent of the cases were greatly improved but not completely freed from pain. It is quite possible that some of this residual pain may yet be found to be due to some unsuspected focus of infection or to mechanical causes and as such relieved. Some improvement occurred in 11.5 per cent, and 6 per cent were not improved. No patients were made permanently worse.

As regards length of treatment, some, of course, were under our care for many months. In those, however, who became symptom-free (65 in number) the following Table shows during which month of treatment the pains finally disappeared, to remain away for at least five months.

TABLE I

Month of treatment	1st	2nd	3rd	4th	5th	6th
Number of cases becoming symptom-free	2	7	20	7	7	7
Month of treatment	7th	8th	9th	10th	11th	12th
Number of cases becoming symptom-free	4	2	7	0	1	1

It will be noted that the third month gave much the greatest number of symptom-free cases.

As regards age, the following Table is revealing. The average age of our 137 patients was 48.

TABLE II

Age	20-30	30-40	40-50
Number of cases	10	22	44
Number of symptom-free results	4	10	24
Age	50-60	60-70	70-80
Number of cases	38	21	2— 137
Number of symptom-free results	19	7	1— 65

Note the number of cases in the decades 50 to 80 when osteoarthritis is common. It will be remembered that osteoarthritis was long held to be due to metabolic, endocrine and mechanical causes, etc., rather than to infection. The fact that it is relieved so frequently by Crowe's vaccine would indicate that it has a common origin with rheumatoid arthritis, i.e., infection.

A study was made to determine at what age a patient had the best chance of becoming symptom-free under vaccine treatment.

TABLE III

Age	20-30	30-40	40-50
Percentage of symptom-free cases	40	45	54
Age	50-60	60-70	70-80
Percentage of symptom-free cases	50	33	50

It is thus seen that our best results were obtained between the ages of 40 and 60, in which osteoarthritis certainly plays a large part.

TABLE IV  
DURATION OF ARTHRITIS AT THE TIME OF VACCINE TREATMENT

Age of patient	20-30	30-40	40-50
Average duration of symptom-free cases before treatment by vaccine	2 yrs.	4 yrs.	5 yrs.
Age of patient	50-60	60-70	70-80
Average duration of symptom-free cases before treatment by vaccine	5 yrs.	5 yrs.	6 yrs.

The average duration of these symptom-free cases before vaccine treatment was instituted was 4.5 years. Seven were from 15 to 20 years.

#### CASE 1

W.W. (No. 7044-33), a female, aged 53, was seen in the medical wards of the hospital suffering from chronic arthritis. The right elbow was very painful and



she could not move it. The fingers were swollen and painful with typical Heberden nodes. On the sixth injection the proper dose was found and she made remarkable improvement, was able to leave the hospital and take up her domestic duties. She is not symptom-free at time of writing, but is so at times for periods varying from one to three weeks.

A metatarsal bar was applied to her shoes on account of metatarsalgia. This gave definite relief to her feet, which had hitherto been resistant to treatment. The depressed anterior arch was here the cause of her pain, and not the arthritis.

## CASE 2

N.B. (No. 17611-28), a male, aged 40, came to the clinic on October 9, 1931, with a painful back. At that time he was unable to bend his back in any direction, and also presented marked muscular spasm. An x-ray, in October, 1931, showed lipping of only the fifth lumbar vertebra. X-ray in May, 1933, revealed condensation of bone over both sacro-iliac joints, more particularly over the left; lipping of both sacro-iliac joints and of the body of the fifth lumbar vertebra.

The Wassermann test was negative. Genito-urinary report—negative. The Laryngology Department reported chronic tonsillitis. Tonsils and adenoids were removed in November, 1931. The teeth were negative.

This patient was our despair, as he was gradually getting worse and was coming to our clinic on crutches. Vaccine was started in October, 1932. At the end of five weeks he had had five days' freedom from pain, the first in years. By June, 1933, he was symptom-free. He had a relapse in September, 1933, but after only five injections became symptom-free again and still is.

This patient had numerous headaches at the start, which gave us great difficulty in determining the dose, but on having his eyes examined it was found that they were the cause. When this was corrected the headaches completely disappeared, and the correct dose was then found, the patient doing extremely well and becoming symptom-free.

## CASE 3

S.L. (No. 11680-32), a female, aged 48, was admitted to the Orthopaedic Clinic on September 23, 1932, with chronic arthritis in right hip and pain in the right wrist. There was swelling of the fingers, with pain.

X-ray report.—Some haziness was noted over both sacro-iliac joints, particularly the left, indicative of osteoarthritis; also lipping and condensation of the bone about the inferior margin of the right acetabulum.

The teeth and throat were negative.

After the twelfth injection this patient became symptom-free, except for the right wrist. A diagnosis of stenosing teno-vaginitis was then made, and she was operated on to relieve the constriction. All pain then disappeared from the wrist and she is able to use it as before.

There are two interesting features in this case. First, it was our first success in relieving the pain and disability due to a definitely arthritic hip joint, and, secondly, the wrist condition, a stenosing teno-vaginitis, over-work of the thumb extensors, was not influenced in the slightest by the vaccine. This helped us finally to diagnose it correctly and cure it.

## CASE 4

L.R. (No. 534-26), a female, aged 42, gave a history of rheumatism for the previous 17 years. She came to the clinic in 1926, and has attended off and on ever since with pain in the right shoulder and both knees.

An x-ray, June, 1926, of left knee, showed lipping of the patella and around the spines of the tibia.

The Wassermann test was negative. The tonsils and adenoids were removed.

She was given foreign protein (boiled milk) with no results. After the twenty-first injection of the vaccine she was symptom-free, except for the right shoulder, which was very painful on movement. She was referred to the Physio-Therapy Department, where the adhesions were broken down by manipulation and massage. Now she has full use of her arm.

This case is of interest as showing how pain may persist in a shoulder (as indeed in any joint) when the active arthritis has come to an end. We were suspicious that her remaining disability was due to adhesions rather than to arthritis. The good result obtained by physiotherapy proved the correctness of our diagnosis.

## CASE 5

E.C. (No. 5432-31), a male, aged 64, came to the clinic in May, 1931, with pain in back, extending down his right leg (sciatica). The history dated back three months. He had had a similar attack in 1925.

An x-ray report May 29, 1931, gave evidence of a marked hypertrophic osteoarthritis involving all the bodies of the lumbar and dorsal vertebrae. This resulted in union between the body of the twelfth dorsal and first lumbar vertebrae, and between the first and second lumbar vertebrae on the right side.

Foci of infection were (1) the teeth, which were all removed; (2) the left antrum (confirmed by x-ray); this was treated. The Heart Clinic reported arteriosclerosis and myocardial fibrosis.

Vaccine treatment was begun on September 20, 1932, and within six months this patient was symptom-free.

His feet gave this patient much trouble. Strapping helped; then his shoes were raised one-quarter of an inch on the inside. This gave complete relief.

Strapping the main arch of the foot, or the application by strapping of a metatarsal pad, or both combined, is a very valuable form of diagnostic treatment. If it gives no relief it is likely that the pain in the foot is due to arthritis rather than to weak arches.

## CASE 6

F.H. (No. 14993-26), a female, aged 50, came to the clinic in January, 1931, with arthritis of all joints; crepitations could be elicited in the knees and shoulders. The elbows, wrists, and ankles were very painful.

She was referred to the Laryngological Department and chronic tonsillitis was reported. The tonsils and adenoids were removed in September, 1931.

An x-ray of the accessory sinuses showed cloudiness of ethmoid sinus of the right side. The teeth were false. A gynecological report was negative.

This patient on two occasions was confined to bed for three and five weeks.

Vaccine was begun in October, 1932. After the ninth injection she could straighten her knee, and after the fifteenth injection became symptom-free.

## CASE 7

A.A. (No. 8370-33), a male, aged 24, came to the clinic on July 12, 1933, complaining of swollen and painful knees and elbows, and pain in the shoulders and fingers.

Definite swelling and crepitations were found in both knees; the elbows were stiff and sore. Vaccine therapy was started on July 14, 1933. The dose that gave relief was found on about the eighth injection.

He had diseased tonsils. These were removed on January 12, 1934.

The genito-urinary report was negative. The Wassermann test was negative. Teeth, negative. The Ophthalmology Department reported on refraction. All the pains in all joints, except the knees, disappeared two months ago. Now the only condition which is retarding progress is fat-fringes, which are to be removed.

This patient is still disabled and walks with his knees somewhat flexed; they cannot be

extended. There is fullness below the patellæ, and pressure here brings on his pain.

For a trial of the vaccine three things are necessary:—

1. The vaccine.
2. Crowe's Handbook, which has to be followed closely.
3. A laboratory where the very concentrated vaccine, as received from England, may be diluted.

We have been very deeply indebted in this work to the other Departments of the Montreal General Hospital. They have investigated, prepared our vaccine, and treated many of our cases and have given us the most invaluable cooperation. Our thanks are heartily tendered to them.

## HICCUP\*

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THE recognition of hiccup, or singultus, by the ancients presents a historical background which dates back to the time of Hippocrates.<sup>1</sup> Their idea of its prognosis may be judged from the following quotations from his "Aphorisms", Libri V, VI, VII, "a convulsion or singultus supervening on excessive purging is a bad sign"; "Singultus and red eyes following vomiting are a bad sign"; "Either vomiting or singultus, or convulsions or delirium following ileus is a bad sign"; and finally "Singultus from inflammation of the liver is a bad sign". Reference is made to its treatment in the "Symposium" in the Dialogues of Plato as follows: Eryximachus, speaking to Aristophanes who is suffering from singultus during dinner, says, "Let me advise you to hold your breath, and if this fails then to gargle with a little water, and if the hiccup still continues tickle your nose with something and sneeze, and if you sneeze once or twice even the most violent hiccup is sure to go."<sup>1</sup> One could quote many ancient references to hiccup, its causation and treatment, but these will suffice to show that the early physicians appreciated something of its importance and attempted its cure.

Hiccup is caused by single or repeated clonic spasms of the diaphragm, with closure of the

glottis. Ordinarily, on inspiration, abduction of the glottis and vocal cords is synchronized with the muscles of respiration so that breathing is a noiseless act. In order to better understand the varied etiology of hiccup a brief review of the physiology of respiration is indicated. The diaphragm is innervated by the phrenic nerves on each side which arise in the neck chiefly from the 4th cervical segment, but also receives filaments from the 3rd, 5th and 6th. In its route to its distribution on the under surface of the diaphragm each nerve is in close relationship to the deep musculature of the neck, the first portion of the subclavian artery, subclavian vein, internal mammary artery, the root of the lung, and the pericardium. The left nerve is also in relationship to the left vagus and the arch of the aorta. In addition to their main function of supplying the diaphragm, all the nerves send filaments to the pleura and pericardium, and probably also to the peritoneum. There is also communication with the sympathetic system in the chest.<sup>2</sup> An accessory phrenic nerve is described by Alexander,<sup>3</sup> occurring in 20 to 30 per cent of cases.

Control of respiration, as you are aware, is of a complex nature, effected through bilateral chief centres in the medulla, with subsidiary centres in the spinal cord. Rhythmic stimuli travel from these centres by various nerve paths

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to the diaphragm, intercostal muscles, glottis, etc., to bring about the synchronized acts of inspiration and expiration. These are automatic in their action, but are influenced by voluntary control. The nerve centres are also affected reflexly by afferent impulses from the pharynx and lungs through the vagi nerves, and from the skin surface generally. In addition, the centres are very sensitive to alteration in the chemical composition of the blood, such as variations in its  $\text{CO}_2$  and  $\text{O}_2$  contents, and to the presence of certain respiratory poisons.

It will be apparent, therefore, that hiccup may be caused directly or reflexly by a great variety of factors, which for purposes of study we may group as follows:—

1. Reflex:
  - (a) affections of the thoracic viscera.
  - (b) " " " abdominal viscera.
  - (c) " " " central nervous system.
2. Epidemic.
3. Neurotic and unknown.
4. Infectious and toxic.

We will consider in detail the various causes under each heading:—

1. *Reflex (a).*—Stimulation of the phrenic nerve or its communications from any source in the neck or thorax, *e.g.*, tuberculous glands, tumour of the lung or mediastinum, lung abscess, pleurisy, pericarditis, or aneurysm.

(b) Similarly, from any stimuli arising in the abdominal area. For example, one of the most common causes is indiscretion in diet—the use of highly seasoned, very hot or very cold food, alcoholic beverages, or the resultant rapid distension of the stomach. This latter is probably the cause of the hiccup one so frequently sees in nursing infants. Hiccup of serious import may arise from strangulated hernia, intestinal obstruction, ileus, carcinoma, subphrenic abscess, cirrhosis or inflammation of the liver, amœbic dysentery, intestinal parasites, appendicitis, and peritonitis; it is of fairly common occurrence following operations on the gastro-intestinal tract, more particularly those involving the upper abdomen, or where there is much manipulation of the viscera. Hiccup ensuing early, usually from the first to the third day, does not carry with it the grave prognosis of hiccup arising later, which is usually significant of peritonitis, ileus or pneumonia.

(c) From stimuli arising in the central nervous system, particularly from brain tumour

or abscess, hydrocephalus, epilepsy, meningitis, cerebrospinal or tuberculous, tabetic crises, brain injury, cerebral hæmorrhage, and epidemic encephalitis. The hiccup which one occasionally sees during anæsthesia is probably also of central origin. One finds no reference to it in the literature, but it may occur at any stage of anæsthesia, is more common during the administration of ether, and cannot be abolished by the use of carbon dioxide or by increasing the depth of the anæsthetic. It is usually very troublesome to the anæsthetist, but is, fortunately, nearly always, self-limited.

2. *Epidemic.*—Hiccup in epidemic form is described by Rosenow<sup>4</sup> who considers it to be a variation of encephalitis lethargica. He was unable to demonstrate any lesion in the phrenic or vagus nerves, but found changes in the brain and spinal cord suggestive of encephalitis. He was able to reproduce the condition in animals with naso-pharyngeal washings from infected cases.

3. *Neurotic and unknown.*—Into this group fall those cases of hiccup in hysterical and neurotic patients which are recurrent, of long duration, and intractable under ordinary treatment. The attacks are often excited by worry, anxiety, fear, or sudden shock in those of suitable temperament. Many cases after exhaustive investigation cannot be ascribed to any known cause.

4. *Infectious and toxic.*—Hiccup is found to occur at times in pneumonia, typhoid, cholera, septicæmia, acute rheumatic fever, chronic nephritis, uræmia and diabetes. During influenza epidemics hiccup is frequently seen, either early in the disease or later during convalescence, and does not appear to bear any particular significance. Mayo,<sup>5</sup> in his recent excellent article on hiccup is convinced of its infectious origin, at least in post-operative cases. He believes in a specific organism, and with Rosenow, he made throat swabs and isolated a streptococcus (*Streptococcus singultus*) which was found to produce diaphragmatic spasm in animals. Men only are affected, usually those over forty-five years of age, and there is a seasonal increase in incidence between November and April. From the number of cases arising after urinary infection or catheterization, he feels that the primary focus is in the prostate.



## THE TREATMENT OF HICCUP

In applying treatment, one must consider the probable etiology of the disease. Those cases due to no serious underlying conditions yield fairly readily to a great variety of remedies, popular and scientific. When these fail and when the patient is seriously ill hiccup becomes one of the most difficult and distressing symptoms with which we have to deal, and at times all remedies fail.

In cases of upper respiratory infection Hart and Matheson<sup>6</sup> report excellent results from spraying the throat with a 2 per cent solution of cocaine, and then applying a 20 per cent solution to the larynx; warm albolene is then slowly dropped into the trachea. Local application to the nasopharynx of menthol or cocaine may also be effectual. Where hiccup is caused by constant direct or reflex stimulation of the phrenic nerve in such cases as mediastinal new growth, diaphragmatic pleurisy, or in reflex stimulation of the nerve from whatever source, the only therapeutic measures of any avail are those which depress the sensitivity of the nerve endings or central nervous system to such a point that conduction is interrupted, or the actual crushing or severing of the phrenic nerve itself. The following drugs should be tried, usually in maximal therapeutic doses,—atropine, luminal, nembutal, bromides, chloral, hyoscine, morphine and its compounds, heroin, nitroglycerin and quinine. The use of sodium amytal intravenously has recently been reported, and the writer has had favourable experience with its administration in prolonged hiccup. A dose of from seven to ten grains is given intravenously, or until the patient becomes unconscious during its administration. Its effect is immediate and usually lasts from two to six hours, when it may be repeated. On account of its tendency to produce pharyngeal paralysis the patient must be constantly, under observation.

Where hiccup arises from the gastrointestinal tract, as is most frequently the case in its simpler forms, removal of the cause is indicated wherever possible. The induction of vomiting often suffices, but, if not, gastric lavage with alkalis should be a routine procedure. Particularly is this true of post-operative hiccup arising early. Following lavage various stomachics or anodynes may be used, such as Tr. Capsici, Tr. Belladonnæ, Tr. Moschi, Hoffman's Anodyne, Chlor-

etone, Benzyl benzoate, Ginger, Peppermint, Chloroform, old brandy, Absinthe, Catnip.<sup>7</sup> Carbo Medicinalis, by virtue of its detoxicating properties, may be tried, particularly in those cases arising post-operatively where partial ileus with toxic absorption may be present. The writer also recommends its use in post-operative vomiting.

There are many simpler expedients which may be effectual in certain cases. Among them are—Valsalva's experiment (attempting to expire forcibly with the glottis closed), sipping ice-water or hot water, traction on the tongue, assuming various bodily contortions, an ice bag, mustard paste, or spraying ethyl chloride on the back of the neck, along the course of the phrenic nerves, or over the area of the insertion of the diaphragm. Blistering of these areas was recommended as early as 1833 by Dr. Shortt,<sup>8</sup> of Edinburgh. Galvanic stimulation may also be used as described in 1897 by Régis and Debedat.<sup>9</sup> The inhalation of ammonia or amyl nitrite is sometimes effectual, and finally pressure on the eyeballs or over the carotid sheath on either side. This latter procedure was described in 1885 by Grognot<sup>10</sup> and in 1892 by Leloir.<sup>11</sup>

There are many advocates of the use of CO<sub>2</sub> alternating with O<sub>2</sub>, which acts by interrupting the respiratory rhythm. Jeffery<sup>12</sup> reports a case of nine days' duration, arising post-operatively and complicated by nephritis, where relief was secured by the administration with a gas machine of a mixture of 30 per cent CO<sub>2</sub> and 70 per cent O<sub>2</sub>. The effect was transient, however, and repeated administration was necessary. Sheldon,<sup>13</sup> using varying percentages of CO<sub>2</sub> and O<sub>2</sub>, reported similar results. Golden,<sup>14</sup> by utilizing a process whereby the patient re-breathed his own expired air, reported success in a case of short duration only. In my experience this method of treatment should be given a trial but is not the panacea it has been claimed to be.

In the infectious type of hiccup, as described by Mayo and Rosenow, these workers prepared an antibody globulin solution which was used in those cases in which they isolated a specific organism, with apparently dramatic results. Their procedure was as follows. After an initial desensitizing dose, 2 to 5 c.c. were injected intramuscularly two or three times daily. In several cases reported one dose was found to

be efficacious in controlling the symptoms. This serum is apparently not available for general use at present.

In those cases of hiccup which do not yield to any definite treatment, or which persistently recur, or are of long duration, or which, *per se*, are endangering the life of the patient, surgery of the phrenic nerve may be resorted to. As early as 1917 Kroh<sup>15</sup> reported the successful treatment by novocaine injection in ten severe cases. Similar results have been recorded by various workers over the past fifteen years, notably Goetze<sup>16</sup> in 1920, and Ghose.<sup>17</sup> Freezing of the exposed phrenic nerve was later reported on by Kroh,<sup>18</sup> and traction on the nerve by Steinke<sup>19</sup> in 1930. In 1921 Kroh first reported the section of the phrenic nerve for persistent hiccup. Several cases where this treatment was unsuccessful are recorded and are probably explained by the presence of an accessory nerve. In recent years surgery of the phrenic nerve in the treatment of pulmonary tuberculosis has become increasingly common and a technique developed which in skilled hands causes little danger to the patient. I feel that a note of caution should here be introduced, because when surgery is resorted to the patient's condition is often critical, and any undue manipulation or shock may defeat the purpose of the operation. The technique of surgery of the phrenic nerve in intractable hiccup is very thoroughly dealt with by Carnes Weekes<sup>20</sup> and Alexander.<sup>3</sup> The former quotes a case report where, following perforation of a duodenal ulcer, the patient developed hiccup which persisted for eleven days in spite of all medical treatment. The left phrenic nerve was crushed with complete relief. Five weeks later the patient developed pneumonia and hiccup returned. Two c.c. of a 1 per cent solution of novocaine were then injected into the right phrenic nerve, which was exposed in its course over the scalenus anticus. Hiccup ceased at once, but returned in eight hours. Traction on the nerve caused but temporary cessation, and finally the nerve was crushed with complete relief. In resorting to surgery one must also bear in mind the wisdom

of paralyzing the diaphragm in cases of hiccup where pleurisy or pneumonia are present, or where pneumonia may ensue, for one must realize that by its action it is chiefly responsible for the aeration of the lung bases.

#### SUMMARY

1. A brief review of the anatomy and physiology of respiration is presented.
2. A classification of hiccup is given, based on its etiology.
3. The various therapeutic agents at our disposal are considered in detail, with particular reference to the use of intravenous sodium amytal, Mayo's antibody globulin solution, Carbo Medicinalis, and surgery involving the phrenic nerve.
4. Caution is urged in the application of surgery on account of the potential risk of hypostatic congestion following paralysis of the diaphragm.

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# A CASE OF *B. ALKALESCENS* (ANDREWES) BACTERIÆMIA WITH SEROLOGICAL CONFIRMATION

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THE scarcity of proved cases of infection by *B. alkalescens* (Andrewes<sup>1</sup>) seems to be sufficient reason for describing a case in which the organism was isolated from the blood stream in pure culture. An added interest is the demonstration of active antibody formation, although agglutination reactions were entirely absent.

Andrewes' original strains were isolated from the stools of convalescent dysentery patients, and their serum did not agglutinate the auto-genous strains. In one such case (a convalescent typhoid patient) I was unable to find positive immunity reactions of any kind. Two definite cases of *B. alkalescens* infection have been described and both were in pregnant women. That of Smith and Fraser<sup>7</sup> was a case of generalized infection exhibiting agglutination of the patient's own organisms and of the type strains of *B. alkalescens* in dilutions of 3,200 and 6,400, respectively, while that of Popoff and Spanswick<sup>6</sup> was a case of pyelitis and cystitis, in which the organism was also isolated from the stools, and had an agglutination titre of 1:640.

## CASE REPORT

In August, 1931, Mrs. W., a widow, 31 years of age, suddenly developed a sharp pain in the right loin, radiating to the region of the right hip, which lasted intermittently for eight days. After this her health was poor, with loss of appetite; she was easily tired and had alternate periods of diarrhoea and constipation until April, 1932, when she had another acute attack of pain, lasting three days. From April to July 12th, 1932, she had a quiescent period during which her general weakness was more marked, terminating with the development of nocturia and frequency of micturition with dysuria, and leading up to another attack of severe continuous pain accompanied by chills and fever. With these symptoms and a fever of 101 to 103° F. she was admitted to hospital on July 14th with a diagnosis of right-sided acute pyelitis and ureteritis with cystitis. In addition, the spleen and liver were both found to be enlarged and tender. During the ensuing week her condition was not improved by urotropin and physiotherapy, and blood cultures and cultures of bladder urine (catheter specimens) taken at this time all yielded *B. alkalescens* in pure culture. The blood Wassermann (taken when febrile) was strongly positive. From July 21st to 25th she showed a subnormal temperature and appeared better, but then developed symptoms of involvement of the left kidney and ureter, and ran a remittent fever of 100 to 101° F. till August 7th.

From August 7th to her discharge from hospital on August 17th she showed steady clinical improvement, despite evening rises of temperature to 100° and small numbers of *B. alkalescens* in her bladder urine. A blood culture was taken on August 17th and proved negative. Serum II was collected at the same time. Subsequently the patient remained in good health and on re-examination on September 14th showed no physical signs of disease. One blood and three stool cultures taken at this time showed no *B. alkalescens* but the bladder urine still showed a few of these organisms. Serum III was collected for special examinations and for a Wassermann test, which was again strongly positive.

*Identification of the organism.*—The strains isolated from this case were compared and found to correspond exactly with Andrewes' original strain of *B. alkalescens*. Their essential characters are as follows. Growth on nutrient agar and blood agar is abundant; the colonies are smooth, moist, colourless, the centres slightly raised and the margins entire. There is even turbidity in broth and no liquefaction of gelatin. In sugar-free media a strong alkaline reaction is produced in twelve hours. Litmus milk shows slight alkalinity in twelve hours and marked alkalinity for the rest of the period of observation (fifteen days). Indol was produced by all strains. The Voges-Proskauer reaction was negative, and H<sub>2</sub>S was not produced. Acid only is produced from dextrose, arabinose, xylose, rhamnose, mannitol and dulcitol; while saccharose, lactose, dextrin, inulin, salicin and inositol remain unchanged.

TABLE I.  
PRECIPITIN REACTIONS

Dilution of Antigen	1:1	1:2	1:4	1:8	1:16	1:32	1:64
Serum I 1:5	5	4	4	3	3	3	2
1:10	4	3	3	4	2	2	1
1:20	3	2	1	1	1	1	0
1:40	2	2	1	1	1	0	0
Serum II 1:5	5	4	4	3	3	2	2
1:10	4	3	3-2	2	2	2	1
1:20	3	3-2	2	2	2	2	1
1:40	3	3	3	2	2	1	1
Serum III 1:5	5	4	3	3-2	2	2	2
1:10	4	4	2	2	1	1	1
1:20	3	5	2	2	1	1	1
1:40	2	1	1	1	1	0	0

0 = Clear; 1 = Trace of opalescence; 2 = Opalescence; 3 = Particulate opalescence; 4 = Finely granular turbidity; 5 = Coarsely granular turbidity. The concentrated antigen (1:1) represents extract from 4,000 million bacilli per c.c.

The above results were only visible after one hour incubation at 37° C. and twelve hours at room temperature. In no tube was a flocculent precipitate found, although a definite range of particulation was seen.



TABLE II  
COMPLEMENT FIXATION

Dilutions of Serum	1:2	1:4	1:5	1:8	1:10	1:16	1:20	1:32	1:40	1:80	Dilutions of Antigen	Strain
Serum I	-	-	3	-	2-3	-	0-1	-	0	0	1:1	Patient's Blood.
	-	-	0	-	1	-	0-1	-	0	0	1:2	
	-	-	0-1	-	0-1	-	0-1	-	0	0	1:4	
	-	-	0-1	-	0-1	-	0	-	0	0	1:8	
Serum II	-	-	4	-	3-4	-	2-3	-	0-1	0-1	1:1	Patient's Blood.
	-	-	3-4	-	2-3	-	2	-	0-1	0-1	1:2	
	-	-	4	-	3-4	-	3	-	0-1	0-1	1:1	Patient's Stool.
Serum III	-	-	4	-	3	-	0-1	-	0-1	0	1:1	Patient's Blood.
	-	-	3	-	2	-	0-1	-	0-1	0	1:2	
Serum II Controls	3-4	3-4	-	3	-	1-2	-	0-1	-	-	1:1	<i>B. alkalescens</i> (Andrewes)
	1-2	1-2	-	0-1	-	0-1	-	0-1	-	-	1:1	<i>B. dysenteriae</i> Flexner (Y. Ledingham)

4=No trace of hæmolysis; 0=Complete hæmolysis; 0-1=Trace of sediment of red blood cells; -=Not tested. The concentrated antigen (1:1) represents 2,000 million bacilli per c.c.

The Michaelis acid agglutination series showed strong agglutination of all the patient's strains at the acid end of the series (tubes 4, 5 and 6) and Andrewes' strain of *B. alkalescens* showed in the order in which the reaction was most marked a similar result. Strains of *B. dysenteriae*, Shiga and Flexner (strain: Y. Ledingham) showed no acid agglutination.

Serum I was taken on August 1st, Serum II on August 17th and serum III on September 14th.

**Agglutination reactions.**—The patient's organisms and *B. alkalescens* (Andrewes' original strain) showed no agglutination with the patient's serum, either macroscopically or microscopically. Living organisms were used throughout, either as broth cultures or as washed suspensions in saline of agar cultures. The dilutions of serum used ranged from 1:1 to 1:2,000, and the temperature at which the reaction was sought varied in different attempts from 50 to 3° C., readings being taken in all experiments up to two days.

**Precipitin reactions.**—The antigen used in these reactions was prepared by the osmotic pressure method for breaking up the bacteria (Murray, 1929) and centrifuging to obtain the clear supernatant fluid. The concentration of the antigen represented an original suspension of 4,000 million per c.c. The tests were controlled by one series of tubes without antigen, one without serum and three series with three different normal sera. None of the control tubes showed any reaction.

**Complement fixation.**—The antigen used in these tests was made by boiling a saline suspension of organisms for five minutes (Nicolle, 1918). The tests were controlled in each series by tubes containing no antigen. In addition seven serum controls were used, including four different "normal" sera, two four-plus Wassermann sera and one serum from a patient with *B. coli* peritonitis. These series gave negative results throughout, except one serum from a "normal" individual which gave a reaction up to one plus in the highest concentration of serum.

#### DISCUSSION

So far as I have been able to find in the literature, only two cases of *B. alkalescens* infection have been reported. That of Smith and Fraser<sup>7</sup> (Aberdeen) is the only other case in

which a bacteraemia was found. The most interesting point in the present case is the lack of agglutination reaction throughout the illness, and the fact that the specific systemic reaction to the infection could only be demonstrated by means of the precipitin and complement fixation reactions. Smith and Fraser, Popoff and Spanswick<sup>6</sup> found good agglutination reactions in their cases, and it is rather remarkable that both cases were pregnant women, whereas the woman whose case is described here was not pregnant.

In the absence of agglutination reactions in this case, it seems possible that infection by *B. alkalescens* may be more common than is supposed, because in most cases, if a positive agglutination has not been observed when testing the patient's serum, the organism has been discounted as a possible pathogen. As both the other cases reported showed the organisms in the stools, and manifested the obstinate constipation of pregnancy, the authors suggested that the constipation might be considered to be the primary cause of the invasion of the urinary system by organisms from the intestine. The present patient also gives a history of constipation and ill health prior to the development of her first symptoms, and therefore the same suggestion as to the source and cause of the infection might be put forward.

The mode of infection of the urinary tract by organisms commonly found only in the large bowel has not been satisfactorily explained, but

in this case there is a proved invasion of the blood stream. The urinary symptoms antedated the symptoms usually associated with a bacteræmia, but it has been shown that even *B. typhosus* can be isolated from the blood stream of contacts many days before the development of any clinical signs of the disease, (Conradi<sup>3</sup>). Therefore it might be postulated that the organisms in this case invaded the blood stream from the intestine, giving no symptoms until they attacked the urinary system.

#### CONCLUSIONS

1. That *B. alkalescens* (Andrewes) is definitely pathogenic.
2. That specific antibodies are formed by the patient and can be demonstrated by complement fixation and precipitin reactions when agglutination reactions fail.
3. That symptoms disappear with the elimina-

tion of the organisms from the tissues and body fluids.

4. That the presence of the organism in the bowel does not give rise to symptoms nor to the formation of antibodies, but supplies the potential source of generalized infection.

The clinical notes on this case were supplied by the courtesy of Dr. D. W. MacKenzie, Head of the Department of Urology of the Royal Victoria Hospital, Montreal.

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### AN ESTIMATE OF THE USEFULNESS OF SOME OF THE NEWER ANÆSTHETICS IN PRACTICE\*

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THE difficult position, into which we are continually being brought concerning new drugs, as it accounts for, so it justifies, an attempt to estimate the usefulness of some of them. It is therefore proposed to discuss briefly those chemical substances which have been employed recently in anæsthesia. If this be done with dueful criticism, whilst it encourages us to proceed, it may help us to improve in our progress.

Let it be taken for granted that the usefulness of nitrous oxide is well known, and let us go on from this knowledge to compare two other gases with it, and so discover their advantages and benefits.

Since the introduction of ethylene as an anæsthetic by W. Easson Brown (1922), of Toronto, and independently by Arno B. Luckhardt and J. B. Carter (1923), of Chicago, this gas has not been used nearly as much as its real usefulness would justify. Exaggerated accounts of explosions have caused such unwarranted fear that the mind of man—even the man on the street—

is still prejudiced. It is true that a degree of incredulity is wise and salutary, but when incredulity becomes an unreasonable pertinacity in face of facts it ceases to be sound. The facts about the explosibility of ethylene are known. Dr. Isabella C. Herb, of Chicago, has published an account of over one million ethylene anæsthesias with no explosions and no deaths (Jan., 1934). Further, it has been reported that twenty ethylene explosions have occurred in the operating rooms of this continent, with one injury and five deaths. During the same time, there have been thirty-nine explosions with mixtures of nitrous oxide, ether and oxygen, with seven injuries and five deaths. Nine explosions have occurred when the gas machine was idle. Two of these were after the use of ethylene and the rest after ether. These comparisons apply with peculiar appositeness. Yet we shall have to wait until the too skeptical minds give up their prejudice. Ethylene anæsthesia is more easily maintained than is that of nitrous oxide; more oxygen may be given, there is better muscular relaxation, the vital functions are not depressed to any greater extent, and recovery is

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just as early, with little or no vomiting, and with the ability to clear the throat. The usefulness of ethylene implies a knowledge of the manipulation of a gas machine, just as is the case with nitrous oxide.

At this point I consider it relevant to admit some apostasy about gas anæsthesia. I used to claim that nitrous oxide might well be given by itself to any one, no matter what the operation. I was convinced of this. But it was only possible in a large percentage of cases by reducing the oxygen supply so considerably that definite cyanosis would be inevitable. In 1924 S. M. Rosenthal and I showed that cyanosis was followed by much greater damage to the liver than is seen after ether is given in the ordinary way (impairment of liver function by a drug may be taken to indicate that all other functions are being concurrently interfered with). Since then I have avoided cyanosis, and do not hesitate to add ether to nitrous oxide or ethylene when it is found that either of these gases is not sufficient in itself to produce the desired relaxation while proper oxygenation is being maintained. In other words, definite and measurable impairment is invariably the result of lack of oxygen. In practice it will be found that when it is advisable to mix ether vapour with ethylene relatively very little will be necessary; that ether may be turned on and off to suit the requirements of a case; and that, toward the end of an operation, the ill effects of ether may be alleviated by "washing out" with an abundance of a mixture of oxygen and carbon dioxide. The usefulness of ethylene as an anæsthetic is unquestionable and constitutes a notable advance in anæsthesia.

Another gas which has just been introduced as an anæsthetic is cyclopropane. It promises to be even more valuable than ethylene. V. E. Henderson and G. H. W. Lucas (1929), of the Department of Pharmacology of Toronto University, were the first to demonstrate its anæsthetic properties in laboratory animals. J. A. Stiles, W. B. Neff, E. A. Rovenstine and R. M. Waters, of the Anæsthetic Department of the University of Wisconsin, have shown its usefulness in man (March, 1934). I have recently heard from Waters that he has had over 1,000 cases, and Harold Griffith, of Montreal, has had more than 300. Both of these anæsthetists are very enthusiastic about the value of cyclopropane. This gas is much more potent than either nitrous oxide or ethylene, 18 per cent being sufficient to produce profound anæsthesia. The degree of

muscular relaxation which it produces, while it is not so absolute as that of ether, is much more complete than that which results from the use of ethylene, and more than that of nitrous oxide. Since 18 per cent is the ample inspiratory concentration of cyclopropane, more than enough oxygen may be used. It may perhaps become advisable to add some inert gas, such as nitrogen, to the mixture of cyclopropane and oxygen. It is reported from the Universities of Toronto and Wisconsin that the pharmacological effects of cyclopropane are such that anæsthesia is produced without the metabolic disturbances which are caused by other anæsthetic agents. This is supported by the recent findings which B. B. Raginsky and I have made, namely, that cyclopropane does not impair liver function nor enhance the damage deliberately produced with chloroform (details of the investigation will be published shortly). Over and above the promising usefulness of cyclopropane in surgery, it appears that its benefits may be applied in obstetrics. Already in several instances I have produced intermittent analgesia as well as continuous anæsthesia during parturition, at the Royal Victoria Montreal Maternity Hospital. The results have been very satisfactory. Here again, the effects of cyclopropane on the liver have been determined and found to be nugatory. These results are to be published separately. The basis of expectation of the usefulness of cyclopropane is so high that it is hoped that its present prohibitive cost will be considerably reduced.

A new ether has been added to our list of anæsthetics, thanks to C. D. Leake, P. K. Knoefel and A. E. Guedel, of the Department of Pharmacology of the University of California. It is vinyl ether or vinyl oxide. It is called "Vinesthene" by the makers, Merck & Company. S. Gelfan and J. R. Bell, of the University of Alberta, were the first to administer it to man (January, 1933). But vinyl oxide has been most extensively used in surgery at the University of Pennsylvania, by S. Goldschmidt, I. S. Ravdin, B. Lucke, G. P. Muller, C. G. Johnston and W. L. Ruigh (January, 1934). Vinesthene compares very favourably with ether and promises to be a valuable anæsthetic. Raginsky and I have studied its effects on the liver and found it quite innocuous. I have used it over two hundred times in obstetrics and unfeignedly believe that it is especially suitable for the relief of "labour pains". The rapidity with which anæsthesia is



induced is most striking, a few inhalations being sufficient; there is very little excitement; any desired degree of muscular relaxation can be obtained; and recovery is very rapid. Respiration is not interfered with as much as when ether is used, and what little circulatory depression does occur is no more than that which is produced when ether is given. Since vinyl oxide is very volatile, it should be used in a closed system with oxygen. A special but simple machine has been devised for this purpose, and can be obtained from the Foregger Company, of New York. However, vinyl oxide may be administered by the "open" method, although with needless waste. Vinyl oxide is so peculiarly suitable to obstetrics that it is not extravagant to predict that it will completely supersede chloroform, the dangers of which it should be our desire to relegate to the past.

Since the introduction of veronal (1903) by E. Fischer and von Mering, numerous other derivatives of barbituric acid have been brought forward. So many have been the disappointments concerning them that I am reminded of an old Bulgarian proverb—"Many an ass has entered Jerusalem". However, I shall avoid trenchant remarks about these treacherous drugs.

While it is true that the barbiturates in therapeutic doses are not ultimately dangerous, and equally true that when only their desired effects are obtained nothing could be more spectacularly impressive, yet all too often idiosyncrasies make themselves manifest in some such form as delayed action, extreme depression, immoderate excitement, or even mania. Although these conditions do clear up, yet, to say the least, they are very embarrassing while they last. We should be warned against the indiscriminate use of this group of drugs. It should be noted that all of the untoward actions of the barbiturates are referable to the brain, and that the other organs and tissues are only slightly affected (as exemplified by a study of the effects of amytal on the liver, kidneys and blood, made by M. Bruger, N. B. Dreyer and myself in 1930). For very good reasons, therefore, I am strongly of the opinion that this class of drugs should be used in small doses as hypnotics or pre-operative medications, and not in doses large enough to produce a condition approaching anything like surgical anaesthesia, with the exception, perhaps, of evipan. In connection with anaesthesia, the use of the barbiturates should be confined to the relief of dread and anxiety. Even so, appre-

hensiveness may be allayed more efficiently by avertin. Perhaps the best use for the barbiturates is to be found in the production of analgesia in the early stages of "labour", combined with scopolamine, which causes amnesia. This combination in comparison with others has been worked out recently (January, 1934) by F. C. Irving, S. Berman and H. B. Nelson, at the Boston Lying-in Hospital. They recommend nembutal as the most satisfactory of the barbiturates. During delivery, anaesthesia should be produced by one of the gases. The last to be introduced (1933), of this group of chemicals, is evipan which, when given intravenously, produces rapid anaesthesia which lasts from 20 to 30 minutes, and promises to be useful for short operations.

It may come to pass that, if many more derivatives of barbituric acid are brought forward, we shall be inclined to quote another Bulgarian proverb—"All these twopenny saints will be the ruin of the church!"

And now, at last, we come to avertin, that bromine substitution product of ethyl alcohol, than which it is less harmful and far more useful, at least in a therapeutic manner. My opinions and convictions about avertin are not of the transcendental kind, for the simple reason that they are susceptible to such positive proof as allows no adumbration of doubt. Incontrovertible data have been published, and still there are those dissidents who will decry avertin. Allow me to give an example of their flimsy reasoning. Because it has happened that some patients have died after cholecystectomy, when avertin was the anaesthetic, there are those who have given the specious opinion that avertin should not be used where there is hepatic disease; they ignore the fact that there is a high mortality in gall bladder surgery at best, and have not compared the effects of avertin with those of other anaesthetics on the liver. This one example is enough to show that it is better to adopt Bacon's inductive method of arriving at truth, based on pure experiment, in order to vanquish the obscurity of preconceived notions.

"Several important actions of avertin have been described:—how it obtunds the nervous system (Eichholtz)—this is the desired therapeutic effect; how respiration is depressed (Anschütz, Specht and Tiemann); how the circulation is influenced (Raginsky, Bourne and Bruger); how the blood becomes concentrated and less alkaline (Bruger, Bourne and Dreyer);

and how the functions of the liver and kidney are somewhat impaired (Bourne and Raginsky). The clinical and laboratory investigations on these actions have shown that avertin, in comparison with other anæsthetics, may be considered practically safe and without contraindication, provided suitable doses are used. So true is this that it seems timely to predict an abiding usefulness for avertin." This is a quotation from a paper entitled, "One Thousand Avertin Anæsthesias", by P. E. O'Shaughnessy and myself. It summarizes fairly succinctly the results of the investigations of several observers.

Avertin is especially indicated in those cases where the patient is nervous, frightened and apprehensive, as in Graves' disease. Here the administration can take place in the patient's room. Due to the fact that this anæsthetic does not produce swelling of the brain, as do others, it has been found to be the anæsthetic of choice in operations upon the brain (J. Dandy, Philadelphia). Avertin may be used repeatedly in the same person to control convulsions such as occur in tetany, or for the performance of painful dressings or examinations (McKim and Bourne). Tolerance to the drug does not develop, and consequently the same dose may be used on

different occasions with approximately equal effects. Avertin does not cause nausea. When it is necessary to use one of the gases alone or with one of the ethers, along with avertin, oxygen may be used more freely than ordinarily, and we know how good a thing it is to use oxygen during anæsthesia. Truly, it may be said that the advent of avertin has enlarged the bounds of anæsthesia in a most beneficial manner.

All of these newer anæsthetics may be usefully and safely employed in combination with one another or with other drugs. For example, it is nearly always advisable to use local anæsthetics with avertin, and frequently necessary to add other general anæsthetics, preferably one or more of the gaseous kind. Perhaps the best argument in favour of combined anæsthesia is that, as smaller doses of each agent are used, the deleterious effects of each will be lessened, and yet the end-result will be satisfactory summative narcosis.

An apposite discussion of the usefulness of some of the newer anæsthetics has been attempted, and in closing I would pay commendatory tribute to those who have done the splendid work during these past ten years—work crowned with such beneficent results that it is easy to foretell further progress.

## SPONTANEOUS SUBARACHNOID HÆMORRHAGE

By W. I. WAITE, M.D.,

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**SPONTANEOUS** subarachnoid hæmorrhage is not readily recognized, and yet, when once seen, the picture is so characteristic that it should not be missed. The extravasation of blood into the space between the pia and arachnoid membranes comes from a superficial vessel, and, except as a consequence of trauma, is almost always from a superficial cerebral vessel. It is met with fairly frequently, since Russel reported a series of 26 cases in the last three years in the Royal Victoria Hospital, Montreal.<sup>1</sup>

### CASE REPORT

F.G., aged 48, male, was admitted to the Brantford General Hospital on March 14, 1933, complaining of severe pain over the right frontal area of his head, extending back into the right temporal and parietal regions. He was restless and irrational at times, requiring morphine. About two weeks before admission, while in Toronto, he had been seized with a moderately severe right frontal headache, which lasted three hours and for which he sought treatment at the Out-Patient

Department of St. Michael's Hospital. A section of a raised ulcerous growth on the left fronto-parietal region of head was removed for biopsy and the pathologist reported the lesion as a squamous-cell carcinoma. Since birth two benign papillomas had been present in this region and about twelve years ago, due to a slight injury, these innocent growths became red and began to enlarge slowly. Six months before admission the rate of growth became much more rapid. At the date of admission the mass was about 2.5 cm. in circumference, raised about 1 cm., with a sessile base and heaped-up margin, and was adherent to the underlying structures. The regional lymph glands were not enlarged. He continued to have a dull ache on the right side of the head anteriorly since the onset two weeks previously. While at work in a machine shop on the day before admission, he had experienced a sudden acute exacerbation of the pain in the right fronto-parietal region. He became faint and nervous, perspired profusely, and 24 hours later was admitted to the hospital in a semi-conscious state.

Shortly after admission he had a convulsive seizure lasting about 30 seconds, during which the left arm and leg were drawn up, accompanied by vomiting and profuse diaphoresis. Following the seizure, the muscles of the left half of the body seemed rigid, and 24 hours later a definite hemiplegia of the left side developed. Kernig's and Babinski's signs were present on the left side. Sensitivity to pain, heat and cold was definitely

diminished over the left half of the body. The right fundus of the eye showed considerable dilatation of the superior and inferior temporal veins, but no hæmorrhages. The margin of the disc was blurred, with a mild degree of œdema. Hearing was slightly impaired on both sides. The blood pressure was 170/110 mm.

Lumbar puncture was performed the day following admission, light ether anæsthesia being required to control the restlessness of the patient. The spinal fluid was found to be under pressure and of a homogeneous blood-red colour; about 20 c.c. were withdrawn. The red blood cells settled out on standing, but did not clot, and the supernatant fluid was of a clear yellow colour. The albumin content was much increased. Following lumbar puncture the pain in the head moderated and the patient became less restless.

Two days later lumbar puncture was repeated. Fifteen c.c. of spinal fluid were withdrawn under slight pressure, which had a homogeneous pink colour. The fluid showed the same characteristics on standing. The patient continued to improve and the paralysis of the left side began to clear up. Lumbar puncture was again repeated three days later; no macroscopic blood was found, but microscopically many red blood cells were present.

The condition of the patient improved rapidly, and when discharged 18 days after admission he was feeling quite well, with no headache. There was still slight œdema of right disc and vision was markedly improved. Reflexes were normal, but sensory impairment was still present, though less marked. Nothing was done for the carcinoma while in hospital but radium will be tried later.

#### ETIOLOGY

The most frequent cause of subarachnoid bleeding is the rupture of a small aneurysm. These aneurysms are much more common than is popularly supposed, being found in 1 out of every 125 in one series of over 5,000 autopsies. Most of them are probably congenital, for they have been found in children as young as 19 months. Hutchison and Baillie<sup>2</sup> claim that they are due to a deficiency of the muscular coat, and are most frequently found at the junction of vessels close to the circle of Willis. Forbus<sup>3</sup> believes that the muscularis of a major vessel develops independently from that of a primary branch. In this way he explains the defect of the muscularis and the frequency of formation of miliary aneurysms at the point of bifurcation of vessels.

Infected emboli, containing organisms of low virulence, as found in cases of subacute infective endocarditis, may produce aneurysms by obstruction of the vessel with subsequent softening of its walls. Subarachnoid hæmorrhages from this origin are often recognized by the added feature of hemiplegia, for the middle cerebral arteries are the most common site of embolism. Syphilis, once regarded as an important etiological factor, is now found to be of little significance. In most series the average incidence has been rather less than 10 per cent.

The condition on rare occasions exists as a complication of arterial hypertension, or it may occur in the course of various diseases, such as typhoid, brain tumour or cysts adjacent to the subarachnoid space. Recently a group of cases has been described occurring in patients with a slight naso-pharyngitis followed in a few days by a subarachnoid hæmorrhage. In these cases a filterable virus was thought to be the causative agent.

In the case reported the presence of a squamous-cell carcinoma upon the scalp raises the question of the possibility of a metastatic lesion in the brain, ulcerating into a cerebral blood vessel and causing a hæmorrhage into the subarachnoid space. However, this is very unlikely. Squamous-cell carcinoma almost always metastasizes to the regional lymph glands. No enlarged glands were found in this case. Hæmorrhage resulting in this way would tend to be more or less continuous. Although the classical signs of brain tumour were present—headache, vomiting, optic neuritis—they cleared up rapidly when the increased intracranial pressure was relieved by lumbar puncture. No cases due to this cause could be found recorded in the literature.

#### PATHOLOGY

The relation of subarachnoid hæmorrhage to the other forms of intracranial hæmorrhage should be noted. From without inwards, hæmorrhage may occur outside the dura mater, as happens in rupture of the middle meningeal artery. Secondly, hæmorrhage may occur immediately inside the dura mater, which occurs in chronic or encysted subdural hæmorrhage. These two forms are probably due to trauma, characterized by the formation of blood clot, are more or less localized, and give rise usually to little or no change in the spinal fluid. The third possibility is subarachnoid hæmorrhage which is in the zone of the spinal fluid, and lumbar puncture readily reveals evidence of the tragedy. The fourth and last possibility is hæmorrhage into the brain itself, as in ordinary cerebral hæmorrhage.

Cases of subarachnoid hæmorrhage are divided into three main groups; those in which sudden profuse unchecked hæmorrhage has occurred, resulting in a speedy fatality; those in which a profuse hæmorrhage has been checked; and those characterized by small re-



peated self-limited bleeding. Post-mortem examination reveals recent blood clot in the subarachnoid space, which often extends into the subarachnoid space surrounding the optic nerves. This latter fact explains the optic signs as seen by the ophthalmoscope.

The presence of blood in the spinal fluid is the most significant of all the findings. This bloody fluid differs in three respects from the spinal fluid found as the result of accidental rupture of a vein. (1) It is intimately mixed with the fluid, so that a series of specimens all present the same appearance; (2) the blood does not clot; and (3) when the red blood cells are allowed to settle the supernatant fluid is of a yellow colour. If the lumbar puncture is not done until some days after the hæmorrhage, no gross blood will be found, but merely the yellow coloration of the fluid known as xanthochromia.

#### SYMPTOMS AND CLINICAL COURSE

The symptoms and signs may be grouped under those due to increased intracranial pressure, those due to meningeal irritation, and those due to the actual presence of the blood itself. The onset is usually sudden. Severe headache soon makes its appearance, and this is followed either by a gradually increasing degree of coma, or by stiffness and retraction of the neck, suggestive of meningitis. Many of the milder cases are diagnosed as encephalitis lethargica. In many cases the preliminary symptoms are mild, the initial attack being followed by apparent recovery. In the case here reported the patient probably had a slight hæmorrhage about three weeks before the severe one. In many cases, perhaps a majority, the condition does not proceed to a fatal termination. The common picture is that of a robust, usually young individual, who is suddenly stricken, with no apparent cause, with excruciating pain in the head, and he becomes

dazed and falls to the ground. His complaints often seem far in excess of what superficial examination would seem to justify. Often he has a slight general rigidity, with some stiffness in his neck and a positive Kernig's sign. The tendon reflexes are usually diminished or absent and the plantar reflex often gives an extensor response. As in the case here reported, there is frequently a transient hemiplegia. Ophthalmoscopic examination will show signs varying from slight hyperæmia to choked disc with retinal hæmorrhage. There is a slight leucocytosis of 11,000 or 12,000, a moderate fever up to 101° F. and occasionally a trace of albumin in the urine.

#### TREATMENT

Treatment of this condition consists in early and repeated lumbar puncture, with removal of sufficient fluid to keep the pressure at or below normal. This gives prompt relief from the most distressing symptoms. Spinal puncture is repeated as long as any blood remains in the fluid, usually 2 to 4 days. The blood pressure should not be allowed to rise, even momentarily, for fear of dislodging the clot in the bleeding vessel and starting a fresh hæmorrhage. This means the patient should be isolated and kept as quiet and comfortable as possible, with the milder sedatives. Cathartics and enemas should be avoided.

#### PROGNOSIS

If treated early the prognosis in most cases is good; if not, it is very bad. One may feel moderately hopeful if the patient regains consciousness in 12 to 24 hours. Repeated attacks are always a possibility.

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**TOBACCO, ALCOHOL AND ANGINA PECTORIS.**—Paul D. White and Trimble Sharber, made an analysis of the past habits in the use of tobacco and alcohol of 750 consecutive private patients with angina pectoris and of 750 individuals without angina pectoris of exactly the same sex and age incidence and from the same walks of life. Comparison shows that 46.1 per cent of the angina pectoris patients had been abstainers from tobacco while 24.4 per cent had used tobacco to excess, in contrast to 37.2 per cent of the control series who did not smoke and 33.5 per cent who smoked excessively. Total abstinence from alcohol was the history

of 64.4 per cent of the cases of angina pectoris and of 61.7 per cent of the control series. Only eight of the 750 patients with angina pectoris (1.1 per cent) drank considerable or excessive alcohol and only one of them drank very heavily, while sixty-three individuals (8.4 per cent) of the control series drank much alcohol, four of them heavily. It appears that neither the use of nor the abstinence from tobacco or alcohol plays an important part in the genesis of angina pectoris. In occasional cases the use of tobacco apparently aggravates or precipitates attacks of angina pectoris and in occasional cases alcohol helps to prevent or to relieve such attacks.—*J. Am. M. Ass.*, 1934, **101**: 655.

## PERFORATION OF THE GALL BLADDER

(WITH A CASE REPORT)

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**PERFORATION** of the gall bladder is a condition met with so infrequently that a report of this case seems worth while.

## CASE REPORT

A.S., a man, 79 years of age, was eating his supper when he was suddenly seized with severe crampy pains in his upper abdomen. He had repeated attacks of colicky pain lasting for 5 to 15 minutes. His physician was called and he gave him morphia which gave some relief. Two days after the onset of his illness he was nauseated and began to vomit. He was admitted to hospital on the fourth day, at which time he was markedly jaundiced. His abdomen was much distended and tender. The result of a van den Bergh test done on admission was 12.5 units. He was very restless, requiring continued sedatives. The distension increased,

gram. Its cut surface was much bile-stained. The largest branches of the portal vein to both lobes were filled with soft thrombus which was fairly firmly attached to the vessel wall. There was considerable dilatation of the cystic, hepatic and common bile ducts, and these showed evidences of acute and chronic cholangitis. There were several small faceted stones in the common bile duct, and one was impacted at its mouth, about which there was considerable thickening. The pancreatic duct showed some dilatation, but was not bile-stained. It opened close to the mouth of the common bile duct. The pancreas was small and deeply embedded in a mass of fat which infiltrated its tissues.

In our records of 2,775 autopsies since 1925, there were 446 cases of chronic gall-bladder disease. Acute cholecystitis was found in 17 cases, while cholelithiasis was present in some 225 cases. In 463 cases showing gall-bladder disease, only 7 showed perforation of the gall bladder, that is, 1.5 per cent. This figure compares closely with those found in other clinics. Mitchell<sup>1</sup> in a series of 1,270 cases of gall-bladder disease which were operated upon, found perforation present in 16 cases, or 1.2 per cent. McWilliams (cited by Blaustein<sup>2</sup>), in reviewing 3,180 operations on the biliary tract, found 29 cases, or 0.9 per cent, with perforation of the gall bladder. Blaustein also quotes Karullon's analysis of 6,114 autopsies in which cholelithiasis was found in 572 cases, 3 of which had perforations, i.e., 1.5 per cent.

Of the 7 cases of perforation of the gall bladder coming to autopsy here, 4 were in males. Traumatic rupture occurred in 1 case. Three had the common bile duct occluded by gall stones and in 2 of these an empyema of the gall bladder was found. Jaundice was present in 3 cases. One case showed an acute suppurative cholangitis with an abscess in the wall of the gall bladder, which resulted in perforation and generalized peritonitis. There was a fistula between the gall bladder and the duodenum in one case, and a large stone had become impacted in the terminal portion of the ileum, giving rise to acute intestinal obstruction and a very extensive ulceration of the ileum, which perforated, the terminal event

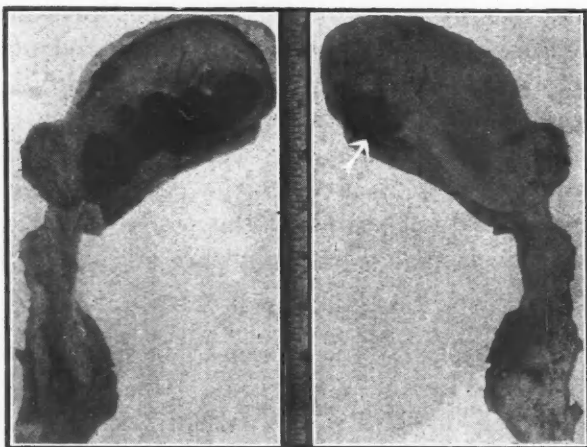


FIG. 1.—Showing interior of the gall bladder and a stone at the mouth of the common bile duct.

FIG. 2.—Showing perforation on the inferior surface of the gall bladder.

and he gradually became worse and died six days after the onset of his illness. The clinical diagnosis was stone in the common bile duct, with a possibility of acute pancreatitis.

At autopsy, the peritoneal cavity contained 700 c.c. of fluid which resembled pure blood. A generalized fibrinous peritonitis was present. Anterior to the great omentum in the left upper quadrant, just below the splenic flexure of the colon, and lying freely in the peritoneal cavity, were six faceted gall stones, the largest measuring 1.5 cm. in diameter. A considerable mass of blood clot was found between the inferior surface of the liver and the pylorus. On the inferior surface of the gall bladder was a ragged perforation measuring 1.5 cm. in diameter. The gall bladder was large and filled with stones together with some bloody bile. The margins of the perforation were ragged and dark red in colour. The wall showed little thickening. Its mucosa was an angry red. The liver weighed 1,600

being a general peritonitis. One case showed a dense mass of adhesions between the gall bladder and the transverse colon. The gall bladder had perforated and a large stone had been extruded. This gave rise to an exogenous ulceration of the colon with perforation and an acute localized fibrinopurulent peritonitis. The stone had not yet found its way into the colon.

Perforation of the gall bladder shows a very high mortality. Mitchell states that the mortality is 43 per cent. Bennett, who is quoted by Mitchell, places the figure at 50 per cent. Probably one of the main reasons for this is the fact that most of the cases in which perforation of the gall bladder occurs have had attacks of colic referable to gall bladder, and in the event of a correct clinical diagnosis they frequently refuse operation, believing this to be another attack of gall stone colic. A correct clinical diagnosis is often very difficult, as perforation of the gall bladder produces no syndrome which one may accept as pathognomonic. Confusion with a perforated duodenal ulcer or with an acutely inflamed

appendix is frequently encountered. However, the condition is usually recognized as an acute upper abdominal condition and at operation a bile staining of the peritoneum is diagnostic.

#### CONCLUSIONS

1. Perforation of the gall bladder is a comparatively rare condition, and is always associated with pre-existing gall-bladder disease, except in cases of traumatic rupture.

2. Clinical diagnosis is very difficult as there are no symptoms pathognomonic of perforation of gall bladder. As a result, confusion with other acute abdominal conditions is frequent.

3. The mortality is high in perforation of the gall bladder and can be decreased only by early diagnosis and operation.

The writer wishes to express his appreciation to Prof. Oskar Klotz for his interest in the preparation of this report.

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### THE USE OF CAUDAL ANÆSTHESIA IN UROLOGY AND PROCTOLOGY\*

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CATHELIN, in 1903, first called attention to the possibilities of blocking the sacral nerves by injecting a 1 per cent solution of cocaine into the sacral canal by way of the hiatus sacralis. The experimental work was done on the dog. Its practical application in the human being failed because the drug was too highly toxic. With the advent of novocaine, Stoekel, in 1909, published the results in a series where he used 30 c.c. of a 0.5 per cent solution of this preparation to relieve pain in labour. His results varied. He called the state "sacral anæsthesia." By using larger amounts of a stronger solution, with the addition of bicarbonate of soda, Laewen, in 1910, was able to obtain surgical anæsthesia for perineal operations. He employed the more accurate name of "extradural anæsthesia." Attempts were then made

by various authors to use larger amounts of novocaine in conjunction with heavy preliminary medication by narcotics, morphine and scopolamine, and so to produce anæsthesia suitable for lower abdominal operations. Some of the patients had complications such as giddiness, nausea and vomiting, delirium, clonic convulsions and death. From some of the histories it would appear that an intravenous injection had been made in some of the fatal cases. As so often happens, over-enthusiasm and lack of skill brought a new procedure into disrepute.

This paper is a presentation of the technique of caudal anæsthesia as we have used it in urology and proctology in private and staff cases, and the report of our results. No claim for anything new or original is made here, but by combining certain features of various technique such uniformly good results have been obtained that we feel this method is of distinct value and merits more recognition. It is an extradural or block anæsthesia and quite dif-

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ferent from a spinal anaesthesia. To make this point clear it will be well to review very briefly the anatomy of the part concerned.

The sacrum in the adult consists of a fusion of five vertebræ, decreasing in size from above downward. It is wedge-shaped, with a dorsal curve. The lower portion of the dorsal surface is subcutaneous, regardless of the muscular or adipose development of the subject. Normally the upper four sacral arches fuse and the absence of the fifth forms the sacral hiatus. The apex of the sacral hiatus is the fourth sacral spine, and the base is bounded by the sacral cornua, which are the remnants of the fifth sacral arch that has failed to fuse. This forms a triangular area with the apex cephalad and covered by the sacro-coccygeal membrane. It is through this membrane that entrance is gained to the sacral canal for the induction of caudal anaesthesia. The important landmarks for caudal and sacral anaesthesia are the posterior superior iliac spines, the tip of the coccyx, the sacral cornua and the fourth sacral spine.

Sometimes the fourth, and, rarely, the third, sacral arch fails to fuse and forms a partial sacral bifida. A complete sacral bifida is the condition where all the sacral arches have failed to fuse. Any such abnormality has an important bearing on this technique, as any defective arches increase the size of the hiatus. The dura mater ends at the level of the second sacral foramen and with any abnormality of the hiatus sacralis there is danger of the needle being inserted too high and the dura mater may be injured or an intradural injection made.

In a study of the dry specimens of the sacrum in the Department of Anatomy, Manitoba Medical College, we were able to review 62 subjects.

TABLE I

	Male	Female	Sex not ascertained
Total reviewed .....	44	9	9
Partial lower sacral bifida..	12	1	2*
Partial upper sacral bifida..	4	0	0
Complete sacral bifida.....	1	0	0

\* One a reputed Indian.

The chief anomalies noted were: (a) Failure of fusion of the upper sacral arches—upper partial sacral bifida. (b) Failure of fusion of the lower sacral arches—lower partial sacral bifida. (c) Failure of fusion of all the sacral arches—complete sacral bifida, Class (a) is re-

corded only as a matter of academic interest, and has no bearing on this paper. The significance of anomalies (b) and (c) has already been noted.

The sacral canal increases in size from below upward and is continuous with the spinal canal of the lumbar region. It contains the dura mater spinalis to the level of the second sacral foramen, a network of lymphatics, a plexus of veins, and some small arterioles, all imbedded in epidural fat. Laterally, the sacral nerves lie in a prolongation of the dura which fuses with the nerve sheath about the middle of the sacral foramina. It is in this extradural space that the anaesthetic fluid is deposited.

#### TECHNIQUE

*Armamentarium.*—This is neither expensive nor elaborate, and consists of one nickeloid unbreakable spinal needle, one fine hypodermic needle, two all glass 20 c.c. Luer syringes, one all glass 2 c.c. Luer syringe, 2 per cent novocain solution.

*Preparation.*—The night before operation the patient is given 5 to 10 grs. of barbital, and this is repeated one hour before going to the operating room in the morning. He may have breakfast unless there is some contraindication in the surgical procedure.

The patient is placed on the table in the prone position and the skin prepared. We prefer mercurochrome or picric acid to tincture of iodine because of the discomfort that any excess of iodine may cause in this region, and also because of its corrosive action on the needles and instruments.

*Injection.*—Having located the sacral hiatus with a small needle and the small syringe loaded with 2 per cent novocain, a cutaneous wheal is raised over this area. After removing the small needle, the spinal needle is now passed through this wheal to the sacrococcygeal membrane. The membrane is punctured and in so doing the point of the needle will probably impinge on the anterior wall of the sacral canal. The needle is then retracted a small fraction of an inch, the heel depressed as the needle is again advanced into the canal 3 to 4 cm.

The stilette is now removed from the needle and note is taken if there is any blood on it or if any spinal fluid is dripping from the needle. Even if this observation is negative, to make assurance doubly sure, a dry syringe is attached

to the spinal needle and suction applied. If blood or spinal fluid is aspirated the position of the point of the needle must be changed to avoid a spinal or intravenous injection. We are now ready to inject very slowly 30 to 40 c.c. of 2 per cent novocain. Any tumefaction of the tissue on the posterior surface of the sacrum, or any marked resistance to the advance of the plunger of the syringe, indicates that the solution is not being deposited within the sacral canal. After the injection is completed a period of at least 20 to 30 minutes is required before anæsthesia is established.

The report of our series is shown in Table II as follows.

that each patient who had had morphine developed symptoms not seen in any other case in the series.

## CASE 1

This patient had perfect anæsthesia for hæmorrhoidectomy, but the effect wore off within the first hour. Morphine was given by hypodermic for post-operative pain and after that the patient had rather a bad time with nausea and vomiting.

## CASE 10

This patient was a doctor up for lithotripsy. He had had the proper pre-operative barbital medication, but either inadvertently, as a hospital routine, or as an added kindness to a fellow practitioner, he was given a hypodermic of morphine before coming to the theatre. He arrived in the operating room quite bright and mentally alert. About 15 minutes after completing the caudal injection he became delirious, and we had to resort to gas anæsthesia, not because of pain but because we could not get his cooperation.

TABLE II

Case No.	Age	Operation	Preoperative medication	Remarks
1.	30	Hæmorrhoidectomy.	Barbital grs. v. H.S. et A.M.	Nauseated after hypo. of morphia. Perfect anæsthesia.
2.	38	" "	" " "	Perfect anæsthesia.
3.	32	" "	" " "	" "
4.	50	" "	" " "	" "
5.	48	Urethral dilatation.	" " "	" "
6.	48	" "	" " "	" "
7.	35	Circumcision and urethral cal.	" " "	" "
8.	73	Crushing stone in bladder.	" " "	" "
9.	70	Cystotomy and cystoscopic	Barbital grs. v in O.R.	Gas for suprapubic; perfect anæsthesia for first part.
10.	70	Crushing stone in bladder	Barbital grs. v H.S. et A.M. Also morph. 1/4 A.M.	Became delirious; had to give gas.
11.	43	Urethral dilation.	Barbital grs. v H.S. et A.M.	Perfect anæsthesia.
12.	25	Cystoscopy; T.B. bladder.	" " "	" " Had been getting morph. Went into delirium.
13.	30	Cystoscopy.	" " "	Perfect anæsthesia.
14.	20	Cystoscopy; T.B. bladder.	Barbital grs. x H.S. grs. v A.M.	" " including lower abdomen.
15.	32	Hæmorrhoidectomy.	" " "	Duration not quite long enough.
16.	32	Cystoscopy; malignant bladder.	" " "	Wide area of perfect anæsthesia.
17.	32	Fulguration.	Barbital grs. x H.S. grs. v A.M.	Perfect anæsthesia.
18.	35	" "	" " "	" "
19.	64	Trans. ureth. prostatic resection.	" " "	" "
20.	42	Cystoscopy.	" " "	" "
21.	22	Lithotripsy.	" " "	" " Inguinal.

A review of these cases is interesting. In no case did we have any suggestion of shock or "the patient going bad", such as one sees in spinal anæsthesia, and which we have also seen in caudal before we began to use barbital in the preoperative preparation. Dr. E. G. Martin, of Detroit, and others have pretty definitely shown that barbital or any of the barbituric group acts as an antidote to the toxic effects of novocaine. On the other hand, morphine seems in some way to be incompatible with novocaine when used in this manner. It will be noticed

## CASE 12

Cystoscopic examination of a small contracted tuberculous bladder. This patient had required morphine for some time to relieve spasm and might be termed a partial morphine addict. He was quite bright when he came to the theatre and went into delirium about 15 minutes after the caudal injection was completed.

## CASE 15

Hæmorrhoidectomy. This was the only case in which the anæsthesia did not last long enough. We got good relaxation and exposure of the parts. There was no pain during the operation, but the man was suffering considerably before the dressing was completed. We are inclined to think this was due to the sacral canal being larger than average and that therefore the solution did not come into as intimate contact with the nerve sheaths as usual.

## CONCLUSIONS

There still seems to be an antipathy to regional anaesthesia. To paraphrase an aeronautic term, the laity and a large percentage of the medical profession are "general-anaesthesia-minded", and it is only by personal experience that either the patient or the doctor can be persuaded that "the old order changeth for the new". The only adverse criticism that we have to offer is that the procedure is somewhat time-consuming, but we feel that this is more than compensated by its advantages.

The use of pre-operative barbitol medication is important, to prevent unpleasant sequelæ and, by the same token, morphine is to be avoided.

We have here a common drug that by this method of administration and in this particular field of surgery fills the requirements of a good anaesthetic — (a) safety, (b) efficiency, (c) economy, (d) no unpleasant after-effects or complications.

Its safety is a particular feature of value in the aged and in associated disease, such as tuber-

culosis. In this class of case the choice of the anaesthetic is often the deciding factor in the success of the surgery to be performed.

The absence of vomiting and straining, plus the cooperation of the patient, are valuable aids in avoiding the complication of post-operative hæmorrhage.

Then in this field of surgery, where electrical equipment is so much used, there is no danger of sparks causing an explosion, and the value of the removal of this fear in a staff educated in the dangers of gas anaesthesia is not to be underestimated.

My thanks are due Dr. Boardman, Chief of Urology of St. Boniface Hospital, for his kindness in submitting suitable material for this series, and to Dr. Inkster, Professor of Anatomy, Faculty of Medicine, Manitoba University, for his help in a special dissection and reviewing the anatomy of this region.

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## OBSERVATIONS ON ACTINOMYCOSIS

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ACTINOMYCOSIS is a chronic infective disease which would appear to be on the increase. From 1920 to 1926, the records of the Toronto General Hospital note the admission of one case. From 1926 to 1931, inclusive, 27 cases are recorded. During the past year there has been an average of one case a month in the wards. While part of this increase may be apparent, due to greater clinical interest, there would seem to be a real increase in the number of cases. Twenty-nine are reported in this paper.

**Bacteriology.**—The majority of cases are due to infection with *Actinomyces bovis*. This is an anaerobic, non-acid-fast streptothrix. Early in the history of the disease it was attributed to one or other of the *Nocardia*. With the recognition of *Actinomyces bovis* the investigation seemed finished. However, an associated bacillus has been identified, whether in a genetic or symbiotic relationship is not yet known. This

bacillus, *B. actinomycetum comitans*, is found in over 80 per cent of cases at some stage.<sup>2</sup>

*Actinomyces bovis* has never been found outside of man or animals. This would seem to absolve grasses as a carrier, a possibility that has been accepted for years. Unless an as yet unidentified stage in the life history of the organism is spent on grasses this absolution must be acknowledged. Transmission from cattle to man and from man to man must occur. There is a fair amount of evidence in support of this statement. It cannot be ignored that 50 per cent or over of the cases occur in individuals associated with farming. Next, there is a case on record of an actinomycotic abscess in the lung of an infant 4 weeks old, dead of marasmus.<sup>3</sup> Falge<sup>4</sup> reports an instance of what would appear to be direct transmission from man to man. Whether the step is a direct one, or whether an intermediate stage occurs is not known.



Some work has been done in an attempt to prove that *Actinomyces bovis* is an inhabitant of the gastro-intestinal tract. Lord<sup>5</sup> claims to have done this years ago, using teeth and tonsils. He came to the conclusion that the organism was normally present in these structures. This does not appear to have been verified, but on clinical grounds it would appear that *Actinomyces bovis* does inhabit the body.

Incidence and location.—

TABLE I.

Author	Male	Female	Total
Sanford & Voelker <sup>9</sup> .....	536	134	670
Sanford & Magath <sup>8</sup> .....	84	12	96
Sanford & Magath (from literature)	79	40	119

TABLE II

	Cervico-facial		Thoracic		Abdominal	
	Male	Female	Male	Female	Male	Female
Cases....	7	4	1	1	13	3
Aver. age	40.7	40.7	48	16	38.1	38.5

TABLE III.  
MALE

Occupations	Cervico-facial	Abdominal	Thoracic
Farmer.....	5	2	0
Student, city.....	0	1	0
Student, farm.....	0	2	0
Gardener.....	0	0	1
Clerk.....	0	2	0
Boat-builder.....	0	1	0
Traveller.....	0	1	0
Press-feeder.....	0	1	0
Salesman, car.....	0	1	0
Smelter man.....	0	1	0
Retired 2 years.....	0	1	0
Agent.....	1	0	0
Garage man.....	1	0	0
Totals.....	7	13	1

FEMALE

Occupations	Cervico-facial	Abdominal	Thoracic
Farmer's wife.....	1	1	0
Wife, city.....	1	1	0
Student, city.....	1	0	1
Stenographer.....	0	1	0 from
Nurse.....	1	0	0 farm
Totals.....	4	3	1

Table II shows the number of cases in each of the three main anatomical groups. The average age is also shown.

The latter half of the third decade would appear to be the favourite age for the development of this disease. The cervico-facial cases included infections of the tonsils, floor of the mouth, tongue, and both sides of the neck. The two thoracic cases both occurred in the left chest. There was 1 upper abdominal infection; 1 abscess in the left lower quadrant. Thirteen cases were associated with the cæcum and appendix, and 1 had its primary lesion in the rectum.

*Etiology.*—Etiological factors are somewhat difficult to evaluate. Nine of the cervico-facial cases had no apparent inciting factor. One patient had had a tooth extracted four months previously to reporting for treatment for an actinomycotic abscess. Eight of the abdominal cases followed acute inflammation in the appendix; this might suggest that the acute inflammation might be a factor in lighting up an actinomycotic infection. On the other hand one patient developed an actinomycotic abscess in the scar of a McBurney incision made 13 years previously for the removal of an acute, ruptured appendix. Two abdominal cases followed injury. In one case the injury had resulted in a retro-peritoneal rupture of the duodenum, from which point the infection had spread. No apparent factor could be discovered in 5 of the abdominal cases. In 2 cases the finding of actinomycosis was incidental in the treatment of an acute appendicitis. It is interesting to note that 24 of the 29 cases occurred in or adjacent to regions normally possessing a high bacterial count, viz., the mouth and cæcum.

One of the thoracic cases followed pneumonia, the other pleurisy. The latter may have been actinomycotic from the beginning.

*Spread of the disease.*—The disease appears to spread, in the abdomen at least, as does any acute infection. From appendix to right sub-phrenic space and thence to the right pleura is a story common to both. It is believed that the infection does not spread by the lymphatics. This observation has been made by many authorities. The neighbouring lymphatic nodes are not enlarged in an actinomycotic infection. The absence of multiple isolated foci leads one to believe that the disease is not disseminated by the blood stream. Direct extension is the com-

monest, and may well be the only, method of spread.

*Clinical syndrome.*—Swelling and soreness are the two main early indications of the disease. In the cervico-facial group swelling was the first sign noticed in 8 of 9 cases in which records were available; the other case had soreness first. As the disease progresses the swelling extends and becomes more tender, although usually not markedly so. Trismus is an early development of cases in the region of the jaw. The involved area is very firm (woody) and is usually of a dull brownish-red colour. The induration fades out into the surrounding tissue. Eventually a soft area in the induration forms, opens, and discharges a thick, greyish pus in which the characteristic granules may be found on careful search. These granules are not always yellowish; two abdominal cases in this group showed granules that were greyish-white in colour. Occasionally the pus is somewhat viscid. Constitutional effects are remarkably constant. Loss of weight practically always occurs. It varied from 10 to 31 pounds in this group, the average being 19. The temperature is characteristically swinging, down in the morning and up in the late afternoon. Ninety-nine to 102° is the usual range. In the cervico-facial group the average white blood count was 10,000; in the abdominal group 14,250. Appetite is variable, but as a rule is not much impaired. The pulse is moderately elevated.

The abdominal cases run a fairly characteristic course. After a variable time following an operation for ruptured appendicitis an abscess points in the operative scar. The finding of a faecolith in such an abscess, or in a persistent sinus, should not be allowed to put one off the track, as in 2 such cases a faecolith was found, only to have the abscess recur. A subphrenic abscess is usually the next development recognized; then abscesses in the abdominal wall, chest, liver; and finally the patient dies with several chronic sinuses discharging on his loin, back, and anterior abdominal wall. The course is usually a steadily downward one, but regressions are not uncommon. Whether these are because of, or in spite of, treatment is not known.

The average duration of symptoms until the correct diagnosis was made was 7 months in the cervico-facial group, 8½ months in the abdominal group. The average duration of life in

the abdominal cases after diagnosis was 4 months.

The following case histories are included in this report since each one has a definite point of interest:

#### CASE 1

R.F., Toronto, aged 16, a waitress, was admitted on July 26, 1928. For one year this patient had swelling of gums and right cheek in the region of the first molar tooth. In March, 1928, she had had four teeth extracted. Following this, swelling and pain increased and a sinus developed on the cheek. The discharge contained *Actinomyces bovis*. Treatment consisted in aspiration, incision, packing of the sinus, 40 grains of iodides per day, and high voltage x-ray therapy. The white blood cells were 18,000. When seen on April 19, 1933, the patient was well.

#### CASE 2

W.B., Summerville, Ont., a farmer, aged 28, was admitted in November, 1931. The patient had had "blind boil" on the left side of the neck at the level of the thyroid cartilage for 3 months. During the week previous to admission the swelling had doubled in size; it was cold, fluctuant and not painful. The abscess was excised widely, the operative field washed with acriflavine and closed without drainage. Bacteriological examination showed *Actinomyces bovis*. This patient has never had a return of his lesion.

#### CASE 3

C.H., Fort William, a farmer, aged 44. This patient was injured in October, 1925. He fell while carrying a heavy piece of wood on his right shoulder. Pain developed in the abdomen and back. After the acute symptoms subsided the right thigh slowly became flexed. On January 13, 1926, more than a quart of pus was obtained from a swelling just above Poupart's ligament on the right side. On February 1, 1926, another abscess ruptured below Poupart's ligament. Two weeks later another abscess formed, and still later another over the back of the right ilium. At post-mortem it was found that the patient had ruptured his duodenum retroperitoneally, which rupture had healed. It was felt that infection had spread from this point through the retroperitoneal tissues. Bacteriological examination showed *Actinomyces bovis* as the causative organism.

#### CASE 4

J. McL., Charlton, Ont., aged 47, a farmer, was admitted on July 15, 1929. In 1916 this patient had a ruptured appendix removed. For six days previous to this admission had had a red, painful swelling in the right lower quadrant. He had lost thirteen pounds in the last few months. At operation a considerable amount of greyish-white pus, containing a great many greyish particles varying in size from the head of a pin to that of a small pea was evacuated. The cavity was the size of a grapefruit with hard fibrous walls and lined with pulpy granulation tissue. The pus was positive for actinomycosis. Treatment was high voltage x-ray, potassium iodide internally, and irrigation of the sinuses with copper sulphate. The white blood cells were 6,200. He left hospital in November with a mass in the right lower quadrant still present. A month later was readmitted for treatment. Pathological examination of material removed at this time was reported as chronic suppuration. The patient reported from Gowganda on February 16, 1932, as "keeping pretty well". He could not be located in April, 1933.

## CASE 5

M.R., Toronto, aged 32, a boat builder. On April 1, 1932, he was operated upon for acute appendicitis. The appendix was reported as showing acute, sub-acute, and chronic appendicitis. His wound healed in five weeks. In July, 1932, his wound opened up again. A faecolith was removed, but the sinus did not heal. In August, 1932, an abscess developed far back in the right flank. Pus from this showed typical yellow granules. White blood count, 9,600. Temperature swinging from 98 to 101.6°. Treatment consisted in incision and drainage, high voltage x-ray, and colloidal iodine. This patient became steadily worse and died in February, 1932.

## CASE 6

W.S., Toronto, aged 40, a shoe traveller. In May, 1929, the patient was operated on for acute appendicitis, perforative. Following this he developed sub-phrenic abscess, and later a right-sided, acute suppurative pleurisy. He was discharged in October, 1929. Three months later was admitted for the treatment of a cystitis. In June, 1931, he was admitted for the treatment of a fistula of five weeks' duration in his appendiceal scar. He was weak and had no appetite. The sinus was explored and a faecolith about the size of a marble removed. The wound was closed without drainage. White blood count, 15,500. Temperature swinging from 98 to 100.5°. In November, 1931, admitted because of cystitis. In March, 1932, he was again admitted with a large painful swelling in the right loin. The abscess was incised and drained, no foreign body or bare bone being found. The wound healed before the patient left hospital. Six months later he was again admitted with another abscess in the right lower quadrant. Pus from this was positive for *Actinomyces bovis*. Treatment consisted of large doses of potassium iodide and high voltage x-ray therapy. January 4, 1933, another abscess in the loin was opened. Healing was rapid. All treatment was repeated. Since then this patient has been in hospital twice for drainage of abscesses. Examination of this man's appendix in December, 1933, revealed the presence of actinomycosis which had not been previously identified.

## CASE 7

F.H., Hamilton, a gardener, aged 41. This patient had pneumonia in November, 1930. In February, 1931, he had a rib resection for empyema. The temperature remained elevated and his cough became worse. The incision was reopened and large quantities of pus were obtained. Again the wound healed. The temperature kept swinging from 99 to 101°. Still later a sinus developed in the chest wall, and in December, 1931, actinomycosis was proved on examination of pus from this sinus. Treatment consisted in potassium iodide internally, and irrigation of the sinus with boracic acid solution followed by the installation of iodine. He died on January 29, 1932. At post-mortem he was found to have been suffering from actinomycosis of left lung and pleura, right and left domes of the diaphragm, liver, spine and retroperitoneal tissues.

**Treatment.**—Surgery, medicine, and radiology all play a part in the treatment of actinomycosis. Surgical procedures include incision of abscesses, curetting of sinuses, and total excision of the lesion. Abscesses must be opened and packed loosely. Actinomycosis seems to prefer muscle, and forms numerous small abscesses which may be entirely separate from each other. Such abscesses must be carefully looked for. Chronic actinomycotic sinuses have walls possessing al-

most the consistency of cartilage, and, to be closed, must be excised.

Iodine is the drug that has been favoured for many years in the treatment of actinomycosis. It has been used locally, by mouth, and intravenously. At first regarded as a specific, its importance has been questioned since the closing years of the last century. In the cases personally observed in this series no definite effect that could be directly attributed to iodine was noted. It is administered in many forms by mouth. Potassium iodide in large doses, tincture of iodine *sine iodo*, and a mixture of cream, milk, and 2½ per cent iodine, advocated by Chitty, were all tried. Diarsenol was given intravenously in one case with no apparent effect.

Radiation therapy was carried out by means of radium packs, the introduction of radium into sinuses, radium needles implanted in the tissue, and the high voltage x-ray.

TABLE IV.

Treat- ment	Cervico- facial	Result	Thoracic	Result	Abdominal	Result
Excision	1	C			1	C
	1	C				
Excision Radium	1	C				
Excision Iodine					1	C
Incision					1	D
					1	D
Incision Iodine					1	D
					1	D
Incision X-Ray					1	D
					1	D
Incision Iodine	1	Dying			1, 1	q D
X-Ray	1	C			1, 1	X q
					1, 1	D D
Incision	1	C				
Iodine	1	C				
Radium	1	C				
Radium	1	C				
Radium X-Ray	1	C				
Radium Iodine	1	C				
Incision			1	D	1	D
Iodine			1	D		
Radium						
X-Ray						

C=Cured; D=Dead; X=Still under treatment;  
q=Not traced.



Locally many drugs were used; the main ones were copper sulphate, iodine, and hygeol.

*After-care.*—After discharge from hospital a careful follow-up of the case should be carried out. The patient should be seen at least every three months. Soreness in or near the area of the wound should be reported at once. This symptom would appear to be the most valuable in warning of more trouble. It may occur a month before swelling develops. A careful record should be kept of the patient's weight.

The methods of treating each case, together with the result obtained, are shown in Table IV.

*Results.*—Nine of the cervico-facial cases were cured, a percentage of 81.89; one is improving and one is dying. Both of the thoracic patients are dead. In the abdominal cases there were two cures (12.5 per cent). One patient is still under treatment 4 years after the diagnosis was made. There were 11 known deaths in this group, a percentage mortality of 68.75. Two patients could not be traced. One of these is known to have been alive and well one year after leaving the hospital. Table V shows the mortality figures for the 29 cases.

A study of Table IV reveals that any case that lent itself to total excision was cured. This

TABLE V.

Result	Number	Percentage
Dead.....	13	44.72
Cured.....	11	37.80
Not traced.....	2	6.88
Dying.....	1	3.44
Improving.....	1	3.44
Under treatment.....	1	3.44

**TREATMENT OF OCCIPITO-POSTERIOR PRESENTATION.**—Analyzing 976 cases of occipito-posterior presentations, G. Melhado argues that subnormal formation of the pelvis does not account for all cases. Anterior position of the placenta, uneven development of the two Müllerian tracts, relaxed pelvic floor, inability of the trunk and shoulders to move forward, as well as inadequate flexion of the head, are all causes of persistent occipito-posterior presentations. The shoulders are commonly fixed by an internal contraction ring. To eliminate this and improve flexion the writer advises interference directly, following full dilatation, the head ceases to advance. His method is manual dilatation of the vagina and careful palpation of the head to make sure of the diagnosis, followed by dislodging the head upwards into the pelvic brim. If a contraction ring is forming it is ironed out. The anterior shoulder is found and pushed well forward.

would seem to bear out the conclusion that the disease spreads by direct extension. In the cervico-facial cases radium appeared to be of definite value, unless, of course, the case progressed to a cure in spite of treatment.

#### CONCLUSIONS

1. Actinomycosis would appear to be on the increase.
2. It is a relatively benign lesion in the cervico-facial region, but is highly malignant in the thorax and abdomen.
3. It appears to spread by direct extension only.
4. Excision is the ideal treatment and should be carried out whenever possible.
5. Radium appears to be of value in the treatment of cervico-facial cases.
6. Iodine is not a specific.
7. Actinomycosis is caused by *Actinomyces bovis* associated with *B. actinomycetum comitans*.

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The head is then placed with the sagittal suture in the transverse diameter and the posterior ear lying in the operator's palm. Along this is passed the lower blade of the forceps, shorter curve facing the occiput, and fitted over the posterior ear. The upper blade is passed over the anterior ear and the pair locked. By gentle rotation the occiput is brought forward and the head into the oblique diameter. These manœuvres are safe, because the head is free above the brim. When it is drawn into the brim again it descends with surprising ease, and is delivered. Criticism of the method is met by stating that neither prolapse of the hand or cord occurred in the series, and that operation above the brim, on a head that has previously descended into it, is quite a different matter to the application of high forceps to a head that had never entered it.—*Am. J. Obstet. & Gyn.*, November, 1933, p. 696.

## CHOREA GRAVIDARUM, WITH THE REPORT OF A CASE\*

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ONE of the truly formidable complications of or conditions associated with pregnancy is chorea gravidarum. To observe a woman with the enlarged abdomen of pregnancy going through the motions of St. Vitus' dance, and to realize that she is soon to face the ordeal of hours of labour is enough to frighten anyone who is faced with the responsibility of bringing her through the parturition and the puerperium. Fortunately the condition is rare. At the Baudelocque Clinic in over 38,000 obstetrical patients it occurred 31 times. Wilson and Preece<sup>1</sup> conclude that it occurs about once in 2,500 deliveries. At the Rotunda Hospital,<sup>2</sup> for some reason, in a series of over 20,000 deliveries not a single case was noted. In the recent book by the Commonwealth Fund,<sup>3</sup> *re* maternal deaths in New York city, 1930, chorea gravidarum is not mentioned as a causative factor in a single case. Yet as early as the latter half of the 17th century, according to Campbell,<sup>4</sup> it had already received considerable attention. The condition is far more common in primiparæ and usually in adolescents. Our case was a primipara, nineteen years old.

There is a good deal of controversy as to whether the disease is toxic or infectious in origin. According to Campbell, from a careful study of the literature and his own two cases, it is an infectious process. He stresses the importance of attention to septic foci. Poynton and Holmes<sup>5</sup> have actually succeeded in isolating the *Diplococcus rheumaticus* from a case of chorea in pregnancy. This would tend to point rather effectively to the theory of infection. Albrecht,<sup>2</sup> writing in 1915, favoured the theory that the condition is a toxæmia, De Lee<sup>6</sup> is apparently inclined to consider it as toxic in origin. Whitmore,<sup>7</sup> of St. Paul, in an article dealing with the neurological aspects in the etiology of chorea gravidarum, points out that at least three-fifths of the cases occur in young

primiparæ to whom pregnancy and the coming labour are an uncharted sea which they naturally face with a good deal of fear.

Dr. Wm. Boyd,<sup>8</sup> though not dealing with chorea as related particularly to pregnancy, thinks that in general in Sydenham's chorea fright is not much of a factor. He states that the incidence of chorea was not increased during the terrifying experiences of the London air raids. John Poynton emphasizes the importance of emotional disturbance at least as a predisposing factor. Mental distress may have been a contributing factor in our own case.

Wilson and Preece,<sup>2</sup> from their truly masterly statistical study based on all cases reported in the literature, and from replies to questionnaires covering in all 951 cases, conclude that it is merely Sydenham's chorea occurring during pregnancy. Berg<sup>9</sup> is inclined to consider chorea gravidarum as a form of toxæmia; this, from observing a case during the last two months of pregnancy which he treated expectantly, with spontaneous delivery. The patient subsequently developed puerperal sepsis with an ultimate localized infected ovarian cyst for which laparotomy had to be performed. The chorea did not reappear post-partum. I believe one would however be nearer to scientific truth in assuming that, while many cases are essentially only Sydenham's chorea, some of them point definitely to being at least partially toxic in origin. Very few cases showed persistence of choreiform symptoms after the termination of pregnancy. Quite a number had no fever during the entire course of illness. These two factors and the improvement shown by at least a few cases following transfusion from healthy pregnant women tends to show that toxæmia is a factor in the etiology of chorea gravidarum.

About half of the cases give a history of previous chorea. Twenty-five per cent of the women with a history of adolescent chorea have a recurrence of the disease during subsequent pregnancies.

\*Read before the Winnipeg Medical Society, December 15, 1933.

The symptoms are no different essentially from those in cases of chorea without pregnancy, varying in degree from a mere restlessness to movements of a more violent character, as in our own case, involving practically all the voluntary muscles necessitating definite restraint. Our own patient, though apparently quite conscious, had to have boards at the sides of the bed to keep her from falling out, at least part of the time. She seemed to try her utmost to be quiescent, but obviously without success. As to the heart,<sup>2</sup> one-third of the cases showed evidence of cardiac disease. Of 46 cases that went to autopsy, in which the heart was examined, 87 per cent showed cardiac lesions. These did not show much in the way of pathological changes in the brain; if any they were in the corpus striatum, and rather mild in character.

According to Jellet and Meddell, chorea has a distinct tendency to provoke early labour. This is not generally accepted. Our own patient did not go into labour spontaneously.

In the treatment we also meet quite a variety of opinions. John A. Hunnicut, Jr.,<sup>10</sup> treated a case of chorea gravidarum by Cæsarean section. He succeeded in saving both mother and child. This was done, he claims, because the patient was in such a condition that any drastic measures seemed justifiable. A more conservative regime is generally the accepted procedure. The free use of bromides, barbiturates, salicylates, Fowler's solution and various forms of iron medication have their advocates. Albrecht is very definite in his assertion that blood from a healthy pregnant woman is of distinct benefit. Sichel<sup>11</sup> found a very material improvement in his case after transfusion of 15 c.c. of such blood on four successive days. Our patient showed a dramatic (I mean for the better) response after transfusions of 20 c.c. of blood from a healthy pregnant woman.

Guynes,<sup>12</sup> because of a fatal termination in a case after the uterus had been emptied, advises early interruption of pregnancy, even in the mild cases, because he thinks that in his own case at least, if he had been allowed to interfere earlier, the result might have been different. Markson,<sup>13</sup> Kaffesieder,<sup>14</sup> Wilson and Preece<sup>1</sup> and text books in general favour conservative measures. Our own one experience would lead to a similar conclusion.

The prognosis for the fetus is stated to give at least a 40 per cent mortality. For the mother it

is approximately 13 per cent fatal. This is a distinct improvement; 56 cases collected by Barnes in 1869 gave a mortality of 30 per cent.

#### CASE REPORT

Mary C., unmarried, aged 19, born in Morris, Man., one of seven children.

*Family history* was essentially negative, except that one sister had had rheumatic fever 3 years before, and another sister, also unmarried, was recently confined at Grace Hospital with her second child. Mary went to school until the age of 13, reaching grade four. She had been in the city since 1927.

*Personal history.*—She gave a history of having had pertussis, parotitis, and influenza; otherwise negative.

*Present condition.*—When first seen in December, 1932, she had no untoward symptoms. In April, 1933, at the Outpatient Department of Grace Hospital she could not tell the exact date of her last menses. She was then apparently six months pregnant, giving a history of no difficulties until just a few days prior to coming to the clinic. She complained of trembling in her hands which at times caused her to drop articles; there were spells of dizziness and insomnia. When examined again a few days later she showed definite signs of choreiform involvement; movements were purposeless and uncontrollable. She was admitted to the observation ward, under Dr. Blondal. The temperature, respirations, and pulse were normal, and remained practically so throughout the illness. Blood pressure 124/86. The heart did not show any evidence of disease. Urinalysis, negative, except for a trace of albumin. The reflexes were all exaggerated. The blood picture was rather striking: hemoglobin, 33 per cent; red blood cells, 3,500,000, blood smear showing marked achromia. The girl was kept alone in a darkened quiet room, but continued quite restless, very irritable, and unable to sleep. There were marked choreiform movements, nearly every voluntary muscle being involved. She was given iron and copper (Ferrosyn) tablets t.i.d.; luminal, gr. 1½, twice daily; aspirin, gr. 15, q.4 h.; Fowler's solution, and nembital, gr. 1½, h.s., but not concurrently with the luminal. This seemed to control her at least part of the time.

When she came under my service on June 1st she was again beginning to show signs of becoming quite restless, complained of marked dizziness, was quite talkative, and had definite auditory and visual hallucinations. I placed her on a salt-poor diet, allowing free intake of fluids, principally fruit juices. Nembital, gr. 3 b.i.d., was given. On the following day, as there was no abatement in the symptoms, we gave her a transfusion of 20 c.c. of blood from a healthy pregnant woman (of course after a preliminary matching). There was a distinct improvement. She was much quieter and slept very well. Another 20 c.c. was given on the following day, and now the choreiform movements and symptoms of nervousness completely disappeared. For about a week she remained practically well, with the exception of some swelling in the left lower limb.

On June 12th marked choreiform movements reappeared. The transfusion of 20 c.c. of blood was repeated, and the condition promptly cleared up. Urinalysis however now showed a heavy trace of albumin and numerous granular casts. I considered that the patient was now definitely over eight months pregnant, and fearing that the nervous manifestations would reappear, causing further exhaustion, labour was induced with quinine and castor oil.

On June 16th she was delivered of a female child in the right occipito-anterior position, weighing 5¼ lbs. The placenta did not come away for 50 minutes following the delivery of the child. Because the bleeding was somewhat excessive, and because we were perhaps somewhat anxious to complete labour, I delivered the placenta and membranes manually; the placenta was at least partially adherent.



(I may here state that shortly afterwards we commenced to use pituitary extract, and most frequently it has been pitocin, in all normal deliveries as soon as the fetal head is born, and we have not seen one such case where we had to wait for the placenta and membranes for more than fifteen minutes.)

The patient made an uneventful recovery; the puerperium was quite normal, there being no further manifestations of choreiform movements or nervousness of any kind. On June 25th blood examination showed hæmoglobin 60 per cent; red blood cells, 4,400,000; colour-index, 68; no abnormalities in the structure of the red cells. Dr. Campbell looked after her in July and had a few septic teeth extracted. I saw her again about a month ago. She appeared to be quite well. The child which at first did not do so well, later, under Dr. Dey's care, progressed nicely.

### CONCLUSIONS

I feel that from a study of the literature, and my own experience with this particular case, the following observations are justifiable.

1. Chorea gravidarum is quite rare.
2. Chorea gravidarum, at least in some cases, is definitely a toxæmia.
3. Transfusions of small quantities of blood

from a healthy pregnant woman are of distinct value in the treatment of this condition.

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## DIABETES MELLITUS IN TWINS

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THE coincidental occurrence of diabetes in twins indicates the probable rôle of inheritance in the etiology of errors of carbohydrate metabolism. References to the existence of diabetes in both members of 20 sets of twins have appeared in the medical literature. In 1914, May<sup>1</sup> alluded to twin brothers who died within two years of each other in diabetic coma. In 1929, Curtis<sup>2</sup> reviewed the records of 13 cases of diabetes in twins. Later, White<sup>3</sup> enlarged Curtis' list by the addition of 5 new cases and, more recently, Peck<sup>4</sup> reported 1 case. Still another example of the development of diabetes in twins is described below.

### CASE REPORTS

F.O. and J.O., aged 56, are identical male twins. Not only do they resemble one another in appearance but their interests, habits and behaviour are remarkably alike. They possess similar physical peculiarities, follow the same occupation, and present comparable clinical records.

In April, 1926, F. consulted his physician on account of a carbuncle on the back of his neck, and for the first time sugar was discovered in the urine. It was ascertained that for the previous 12 months he had been losing weight and strength, and that during the three months preceding the onset of the infection

the weakness had been noticeably more pronounced and was accompanied by an unusual thirst and the passage of an abnormal amount of urine, especially at night. He had always been an exceptionally hearty eater and had been addicted to the use of alcoholic beverages to excess. A diagnosis of diabetes mellitus was made. He had suffered an attack of diphtheria when 7 years of age, and had contracted gonorrhœa at 25. He had been myopic always.

At the time of his first admission to the Victoria Hospital, London, in April, 1926; the urine contained an abundance of sugar and moderate amounts of ketone bodies. The blood sugar was 290 mgm. per cent and the Wassermann test was negative. Physical examination revealed a well-nourished, rather obese, man suffering from a painful, inflammatory, indurated swelling, about five cm. in diameter, on the back of his neck. No other focus of infection was discovered. The temperature was 101° F.; the respirations were 20; and the pulse rate 100 per minute. The blood pressure was 140/70 mm. Except for the presence of a considerable degree of myopia, no other physical abnormality was found. A culture of the pus from the site of the infection gave a pure growth of *S. aureus*. Following drainage of the abscess and the institution of dietary and insulin therapy, rapid improvement in the diabetic condition occurred. When he was dismissed from the hospital a month later he was receiving 30 units of insulin a day and a diet composed of 45 gm. of carbohydrate, 100 gm. of protein, and 110 gm. of fat, with a total food value of 1,570 calories. On this regimen his blood sugar was maintained within the normal limits and the urine was sugar-free and acetone-free. The lesion on the neck had healed.

After leaving the hospital, he failed to follow instructions regarding his diet and the use of insulin, with the result that he experienced a return of the diabetic symptoms, and, in addition, had occasional attacks of precordial pain, especially following exertion.

In July, 1931, he was re-admitted to the hospital in a pre-comatose state with ketosis, from which he recovered following adequate therapeutic measures. He was 30 lbs. lighter than at the time of his previous admission. At the end of a fortnight he was discharged, with the recommendation that he take 22 units of insulin daily and a diet consisting of 140 gm. of carbohydrate, 80 gm. of protein and 100 gm. of fat, which supplied 1,780 calories. In spite of his failure to adhere to this prescribed treatment, he has managed to avoid, up to the present, the major complications of his disease.

At the time of the discovery of F.'s diabetes in 1926, the attending physician, aware of the possible significance of the remarkable similarities between the patient and his twin brother J., suggested that the latter also submit a sample of urine for examination, although he was free from symptoms. It was found that J.'s urine gave a positive test for sugar, almost as marked as that of his brother. His history is extraordinarily like that of his twin. For example, his habits of eating and drinking were similar to those of F. He contracted gonorrhoea when 22 and diphtheria when 40 years of age. He, too, has been myopic all his life. It is of interest to note that the father and a sister of these twins had the same type of ocular defect. Although the use of an anti-diabetic diet was recommended following the discovery of the glycosuria, he paid little heed to the advice, with the result that his condition became progressively worse, until, in 1929, the symptoms of weakness, thirst, polyuria and nocturia were pronounced. He suffered from furuncles on the back of his neck and periodic attacks of precordial pain.

On admission to the Victoria Hospital in November, 1930, his blood sugar was 285 mgm. per cent and the urine contained a large amount of sugar, but no ketone bodies. The Wassermann test on the blood was negative. He weighed 159 lbs., as compared with 172 lbs. in 1928. Nothing remarkable was discovered on physical examination with the exception of a marked degree of myopia. The blood pressure was 150/100 mm.

When, eight days later, he was dismissed from the hospital, the 24-hour urine was sugar-free, and he was receiving a diet composed of 90 gm. of carbohydrate, 84 gm. of protein, and 112 gm. of fat, providing 1,704 calories, together with 26 units of insulin per day. Like his brother, this patient has shown marked indifference regarding the proper management of his case and has followed instructions only intermittently. Withal, he has avoided the more serious hazards which endanger the course of the severe diabetic.

As far as it was possible to ascertain by careful questioning, diabetes was non-existent in the relatives of these brothers. However, information regarding the family incidence of diabetes acquired in this way is apt to be incomplete, as pointed out by Sherrill,<sup>5</sup> who found that out of 40 relatives of 23 diabetics who had no suspicion of diabetes in themselves, more than one-half showed impairment of carbohydrate assimilation when investigated by means of the glucose tolerance test.

#### DISCUSSION

The occurrence of the same disease in more than one member of a family is suggestive of an hereditary factor associated with the affection. The development of the particular disease at approximately the same age in different members of a family is evidence favouring the hereditary nature of the disorder, as has been emphasized by M. T. Macklin.<sup>6</sup> The onset of the abnormality at approximately the same age in identical twins, who originate presumably from the same germ cells, should be still more evidence in favour of an hereditary influence in the causation of the malady. The frequent observation of similar pathological conditions in twins affords grounds for speculation from the standpoint of human constitutional susceptibilities, as pointed out by Margolis and Eisenstein.<sup>7</sup>

While diabetes can not be ascribed to a single cause, practical experience, as well as the results of certain special observations and theoretical considerations, indicate that there is undoubtedly an hereditary element operative in many cases of the disease. There are reasons for believing that the tendency to diabetes may exist as a Mendelian recessive characteristic in some families and as a dominant characteristic in others.<sup>8, 9, 10</sup> According to several authors who have written on the subject of heredity in diabetes, there are indications of an inherited tendency to the disease in from 30 to 40 per cent of cases. Whether a so-called inherited tendency is sufficient to account for the development of active diabetes without the aid of contributing influences is uncertain. Doubtless, many cases are the outcome of the combined effects of a pre-disposed susceptibility to the disorder plus one or more activating causes.

Inasmuch as twins are subject frequently to similar environmental as well as to similar developmental influences, it may be contended that sufficient explanation can be provided to account for the onset of diabetes in these individuals on the grounds of similar infections, gastronomic habits, or degenerative processes. While such possibilities warrant deliberation, it would appear that the onset of the disease in twins depends upon some more fundamental factor, as a consideration of the data compiled by White<sup>3</sup> indicates.

Dizygotic twins (also known as di-oval, dis-

similar, or fraternal twins) are formed from two distinct ova which are fertilized either simultaneously or successively. Twins of this type may or may not be of the same sex and, as a rule, they exhibit no more similarity to each other than that which may exist in ordinary brothers and sisters. Monozygotic (mon-oval, homologous, or identical) twins are formed by the complete division of one fertilized ovum into halves, each of which develops into an independent child. These individuals are always of the same sex, frequently exhibit similar characteristics and, of course, possess identical inheritable qualities.

In the general population, dizygotic twins are encountered three times as frequently as monozygotic twins.<sup>11</sup> If environment were the principal cause of diabetes in twins there should be no reason to suspect a deviation from the natural 3 to 1 ratio with regard to dizygotic and monozygotic types among the cases which have been reported. However, the recorded observations indicate that practically all diabetic twins are of the monozygotic variety. Of the 21 pairs on record, including the one described in this paper, the sexes were the same in 20. Of these 20 cases, 15 were evidently monozygotic, and only 1 dizygotic. While no information as to identity was supplied in the remaining 4 cases, the fact that the sex of each pair was the same would make it seem reasonable to assume that they also were monozygotic. Thus, the great majority of twin diabetics are of the monozygotic type and, therefore, the individual members of each set possess an identical hereditary background. There was a positive family history of diabetes in 6 of the 21 reported cases; a negative family history in 12 and no mention of familial incidence in 3 cases. Had special methods of investigation been employed for the purpose of detecting abnormal carbohydrate metabolism in the relatives of these cases, as referred to above, the familial feature might have been more striking.

If inheritance is an important causative factor in diabetes in twins, it may be argued that the disease should become manifest at an early age and at approximately the same time in both members of any given set of twins. In 4 of the reported cases, the diabetes began before the age of 15. The youngest age at which it developed was 3 years; the oldest 67.

It was diagnosed simultaneously in 5 sets of twins and in the others, the time interval varied from a few weeks to as long as 48 years. In the majority, however, the disease was detected within a comparatively short time in both members of the various sets of twins. Assuming a predisposition to diabetes, the actual development of the malady may be precipitated by a variety of conditions such as infections, toxæmias, over-eating, obesity or arteriosclerosis, which influences need not be operative at the same time or to the same degree of intensity in each member of a set of twins. Presumably, the effects of these various exciting factors occurring at different times in the lives of the individuals could account for the differences of age at which the diabetes was first discovered. It will be noted that in the case of the twins described in this paper, whose life histories were practically identical, the diabetes appeared at the same age in each; also, that the degree of severity of the disease was the same in each, as indicated by the nearly identical initial blood sugar concentrations and the similar insulin requirements.

#### SUMMARY

An example of diabetes mellitus developing simultaneously in identical twins is described. The addition of this case to those reported in the recent literature brings the total number of recorded instances of diabetes in twins to 21. The question of hereditary predisposition as an etiological factor in diabetes is discussed.

The author wishes to acknowledge his indebtedness to Dr. D. A. Cameron, of London, Ont., in whose practice the above-described cases occurred, for permission to report their case-histories.

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## Case Reports

### AN UNUSUAL TERMINATION IN A CASE OF TUBERCULOUS SPINE

By R. W. KIRKBY, M.D.,

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J.C., a Chinese male, aged 31, was admitted to the services of the Saskatchewan Anti-Tuberculosis League at Saskatoon on October 10, 1929, for tuberculosis of the seventh cervical spine. He was treated by bed-rest, and cast, etc., but left against advice before treatment was completed. He was admitted to the services of the Prince Albert Sanatorium on September 23, 1933, because of a new spinal lesion at the fifth lumbar vertebra. The patient was quite toxic on admission; pulse 112-130, and temperature 101-104°, with a tendency to remain at the higher level until he died on December 15, 1933. His clinical course was dominated by gastrointestinal symptoms for which no adequate explanation was obtained until post-mortem. On December 3rd a fluctuant mass was apparent in the right lumbo-sacral region from which 42 c.c. of smoke-coloured pus was aspirated. This had a very offensive odour suggesting *B. coli*. The laboratory report showed organisms to be gram-negative rods belonging to the *B. coli* group.

The patient rapidly became weaker and was apparently close to death when, on December 10th, he had a number of hæmorrhages of bright red blood from the bowel. These continued for the next forty-eight hours. He died apparently as a result of toxæmia and debilitation from loss of blood.

The post-mortem showed an adhesion of the mesentery down over the front of the abdominal viscera generally. There was destruction of the lower part of the fifth lumbar vertebra and the adjacent intervertebral disc. An abscess was present in each psoas sheath which contained more than a cupful of pus. This was of the same nature as that aspirated from the right dorsal region. There was an adhesion of the sigmoid to the surface of the psoas abscess and an ulcerative process of the intestinal wall. Two small hæmorrhagic spots marked the site of the bleeding. The colon above the adhesion was

quite distended with three or four times the usual bowel content. Death was materially hastened by hæmorrhage from the bowel, but was mainly due to the toxæmia from a pair of mixed infection psoas abscesses in which intestinal organisms predominated. No sinuses were present.

### A CASE OF INFESTATION WITH DIPHYLLOBOTHRIUM LATUM

By W. B. McCLURE, M.B., D.P.H. AND

LUKE TESKEY, M.B.,

*Toronto*

Infestation with the fish tapeworm has very occasionally been found in Toronto. From June, 1926, to December, 1932, in the Toronto General Hospital 6 cases are recorded. The case recorded here presents several interesting features, and is presented in the hope that other cases may be reported, and an endeavour made to determine whether any native cases are to be found in Toronto.

#### CASE REPORT

*Clinical history.*—Mrs. L.M., aged 27, a fairly well developed woman, was born in Vlaama, Finland. Her father was a fisherman and fish was a constant article of diet in the home. At the age of 6 years she passed segments of tapeworm and was treated by home remedies. At 15 years of age, although she had not been entirely free and continued to pass segments of worm, she again took medicine from a drug-store. From that time until the present she had passed segments of tapeworm about every 6 weeks. She had periodically taken medicine without a doctor's advice. Four years ago she came to Toronto and had lived here ever since. She stated that at no time had she eaten raw fish in Canada, nor did she care to taste it in any way in the raw state. Fish was usually eaten by the family once a week. They cooked their own meals and lived in rooms. There was no history of infection in the husband.

The patient came to my (L.T.) attention about 6 months ago and went through a normal confinement. She was able to feed her baby for about 2 months and then had to supplement

the feeding. At 4 months she weaned the child. No mention was made of the tapeworm until January 10, 1933, when a specimen was brought to the office for diagnosis.

*Treatment.*—She was instructed to take a saline purge in the morning. She fasted throughout the whole day, being allowed only orange juice and water. The following morning she was given filix mas in one c.c. capsules for 8 doses, starting at 7 a.m. These were taken at 10-minute intervals. Two hours after this she passed a large amount of tapeworm. Throughout the day she continued her fasting and repeated the medicine on the following morning. There was no further evidence of tapeworm segments being passed.

*Laboratory findings.*—On January 23rd, part of a cestode worm, several feet in length, was received at the Provincial Laboratory. The proglottides measured 8 mm. by 4 mm. The uterus was lobulated and centrally placed. In front of it was the vaginal orifice and in front of this the orifice of the cirrus. The testes were disposed in the lateral fields. The ovaries were behind and lateralward to the uterus. A diagnosis of the proglottides of *D. latum* was made.

On January 26th a second specimen was received in a pint glass sealer which was about three-quarters full of worm. The total length of these segments was approximately 140 feet. The largest segments were 6 mm. by 2.5 mm. and the quadrate segments were 6 mm. by 4 mm. The specimen was carefully gone over and two scolices were recovered. They showed the typical suckorial grooves of *D. latum* and were 2.5 mm. by 0.75 mm.

*Blood picture.*—Red blood cells, 3,550,000; white blood cells, 5,800; hæmoglobin, 70 per cent.

*Differential count.*—Polymorphonuclears, 38 per cent; large lymphocytes, 19 per cent; small lymphocytes, 38 per cent; eosinophiles, 2.5 per cent, transitional cells, 2.5 per cent. The blood smears showed a definite irregularity in the size and shape of the red blood cells. An occasional poikilocyte was found present. No normoblasts were seen. On March 20th a specimen of stool was submitted and the ova of *D. latum* were still found.

#### SUMMARY

A case of infestation with fish tapeworm is described in which over 140 feet of worm and 2 heads were recovered in the stool after a vermifuge had been given. The patient presented an anæmia of a moderate degree.

#### DORSAL DISLOCATION OF THE WRIST WITH FRACTURE OF THE RADIUS: REDUCTION UNDER LOCAL NOVOCAINE

BY W. H. IRVINE, M.D.,  
Fredericton, N.B.

On April 3, 1933, Mr. T.S., while cranking his Ford sustained a typical Colles' fracture along with complete backward dislocation of the right wrist. Reduction was effected under the local application of a 2 per cent novocaine solution, which provided complete anæsthesia. The arm was put up in plaster, etc., and he continued daily to drive his car and deliver his milk to his customers. The case was so perfectly satisfactory and the patient so benefited that it is felt that the good news should be passed along, for with free use of such means, plus the fluoroscope and x-ray confirmation, one could ask for nothing more ideal.

A preparation which acquired a world-wide reputation in the eighteenth century, and which is still employed, is the well-known "Dover's Powder." It was invented by an adventurous sea-captain named Thomas Dover, who was born in 1660.

Part buccaneer and part adventurer, he had a remarkable and romantic career, and is said to have been the rescuer of Alexander Selkirk, the prototype of the immortal Robinson Crusoe, from the island of Juan Fernandez in 1709. After retiring from the sea, he settled down in London in 1728 to practise medicine, and in a chapter on gout in a book he published, he

gave the formula for a "diaphoretic powder," consisting of opium, potassium nitrate, vitriolated tartar, liquorice and ipecacuanha, which he found to be very effective in that disease. This powder, which became known as "Dover's Powder," was largely used in the treatment of fevers, and proved of such value that it was eventually made official in the London Pharmacopœia under the name of Compound Powder of Ipecacuanha. Modifications have since been made in the formula, and it still remains an official and valued preparation.—C. J. S. Thompson in "The Mystery and Art of the Apothecary, p. 247.

## Editorial

### THERAPEUTIC IMMUNIZATION IN STAPHYLOCOCCUS INFECTIONS

ALTHOUGH it is not possible to select and evaluate correctly all the relevant observations and inferences bearing on therapeutic immunization to be found in the literature on staphylococcus infections, a useful purpose is served when one of sufficient experience makes a clear statement of his interpretation of the available evidence. This is particularly so when it is possible to encourage the development and use of procedures founded on sound work and proved to be of value in their application.

Recent work, especially that of Dr. Claude Dolman, of the Connaught Laboratories, Toronto, justifies an article with the above title, since the application of existing knowledge has given results which indicate that it is now possible to relieve a deal of suffering, and that an important line of inquiry has been developed which should be encouraged. In spite of these good and sufficient reasons for the writing of this leader it must of necessity be unsatisfactory; for not only is everyone's experience limited and his reading incomplete, but the imperfection of our understanding of the processes involved looms largely in the picture and "when you don't understand what you're talking about it's so difficult to know what to leave out".

It is important to realize that staphylococcus infection is one disease only, with a variety of clinical manifestations, ranging from the most trivial to the most severe; due to the route of infection chance dictates, to the degree and method of dissemination of infection in the body, to the sites of localization, to physiological variations in different strains of the organism, and to variations in degree of what may for convenience be called resistance or susceptibility of the patient. So it happens that in its various forms staphylococcus infection comes under the care of almost all of the many subdivisions or specialties in medical practice and accordingly receives almost as many names. This variability in the disease is forcibly expressed by the abrupt evolution of one form from

another, irrespective of duration, and by the serious change in prognosis that may result. At the same time, few infections are so persistent as certain staphylococcal lesions of the skin or bones, and few are so prone to reappear when there seems every reason to suppose that a cure has been effected; while at no time is the patient free from danger of the infection assuming one or other of its more serious forms. It is true that the disease may, as it were, fade out for no obvious reason, but there is no convincing evidence that the natural infection produces a sufficient protective immunity, while there is some reason to suppose that a predisposition to further infection develops. The disability, the disfigurement, suffered in so many cases, and the ever present threat held in the strikingly high mortality of staphylococcus septicæmia, multiple pyæmic abscesses or meningitis, make welcome any advance in knowledge from which we may hope for some certainty of control, if only in a proportion of cases. Our real purpose now is to draw attention to the fact that an advance of this nature has been accomplished.

Space does not permit an analysis of the literature dealing with the study of staphylococcus toxin and the production of anti-staphylococcus serum; the curious will find many interesting observations in the writings of a number of investigators from 1891 onwards, and, be it said, several of the earlier observations suggest lines of research which might well be followed with advantage. Up to 1929 the only effective immunity process available was a vaccine, consisting of a suspension of killed staphylococcus culture. There is no doubt that cures have been effected occasionally by vaccines, quite irregularly, in minor, though often persistent, cases of staphylococcus infection. This uncertainty has not been accounted for, and, although reasons for it might easily be deduced from what is known of the organism and its physiology, nothing is gained by guessing. The year 1929 also limits the period of haphazard production of anti-



staphylococcus sera, none of which shewed any promise of therapeutic usefulness.

During the last five years, arising mainly out of Burnet's work, it has been possible to obtain a very active true toxin from staphylococcus cultures, and it would seem at present that this toxin is sufficient to account for the main features of the lesions in all types of staphylococcus infection. It is reasonable, therefore, to expect satisfactory clinical results when this toxin is used either for active immunization in minor cases or for the production of antitoxic serum for passive immunization in severe cases. The results described by Dolman, using one or other of these methods in cases of almost every variety, realize this expectation to a degree which is most satisfactory at this early stage of its trial. There seems to be no reason to doubt that in this absolutely specific method of treatment, the production of a true antitoxin, we have the means of reasonable therapeutic control of staphylococcus infection.

The therapeutic application of active immunization takes advantage of the fact that the toxin treated with formaldehyde loses its injurious properties without diminution of its power to stimulate the production of antitoxin. This preparation called "anatoxin", or, more unfortunately, "toxoid", seldom causes any marked local or general reaction, and its most surprising property is the unexplained rapidity with which it produces a therapeutic effect in suitable cases. Considerable care has to be exercised in its preparation to ensure safety in its use and effectiveness in its results; these are problems for the bacteriologist, and it is hoped that a method of standardization will be introduced soon, to safeguard against commercial exploitation and disappointment to those who have to rely on commercial products. The simplicity of its use is a great advantage, but it cannot be emphasized too much that it is completely specific, that it is only effective in staphylococcus infection. Therefore it is always well to control the cases by adequate bacteriological examinations.

Theoretically, for the treatment of severe cases of staphylococcus infection it is desirable to have available a potent antitoxin; this is the serum of a hyper-immunized animal, preferably concentrated and purified,

as far as is practicable and permissible, to contain the largest amount possible of antitoxin in a small volume. The remarkable series of cases published by Dolman (this *Journal*, page 1) bears out this hypothesis, and, in spite of his very conservative statement, if individual cases are considered, the results surpass any reasonable expectations. Previous attempts to prepare and use staphylococcus antitoxin have not been reported as particularly encouraging. A series of cases treated with serum from one source proved disappointing in my hands, whereas I am convinced that the Connaught Laboratory serum I have been privileged to use has been the major cause of recovery in several cases in which the initial outlook was hopeless.

The employment of serum, such as that produced by the Connaught Laboratories, good as it is, presents certain difficulties characteristic of serum therapy, in addition to those inherent in the case to be treated. In a general way, however potent the antitoxin may be, it cannot undo any damage already suffered by organs and tissues; it is only able to protect from further damage. Therefore, serum treatment used alone can only be expected to be completely sufficient in cases where no extensive metastatic lesions have developed. In other cases it very definitely makes surgical intervention possible, when it would otherwise not be so, by preventing extension of the lesions and allowing of good encapsulation of abscesses. In these cases the antitoxin can clear the blood stream in septicæmia, prevent fresh localizations, and, by protecting the young growing cells, greatly assist the healing of old lesions, but free and adequate surgery is absolutely essential in every case, in addition to treatment on general principles.

Patients to whom staphylococcus antitoxin is all important are naturally extremely ill and in grave danger, so it is important to realize that intravenous administration of the serum is the most effective procedure. But, as it is attended by severe "shock", which is a very serious strain on the patient, this method should be regarded as of a major character, and we have found a prolonged general anæsthetic of great value in saving the patient from the serious circulatory, pulmonary and other disturbances. At the

same time the anæsthetic safeguards against anaphylactic manifestations. The intramuscular route has disadvantages in that the antitoxin is absorbed very slowly, and if the patient is sensitive to horse serum the antitoxin is "fixed" at the site of injection. It is therefore advisable to desensitize every patient carefully. This route has been shewn to be of value if sufficient of a highly potent serum is used. The cases presenting the greatest difficulty are those with lung abscesses, and much has yet to be learned of the management of them. Extensive osteomyelitis also has troublesome features, and the surgical management of the local lesion

seems to need further study, even though the patient's general condition can be improved and complications controlled.

A study of Doctor Dolman's paper will reveal that an important advance has been made in the treatment of staphylococcus infections, which, on its own merits, cannot be neglected. Only, and this is a proviso of great importance, if the best results are to be obtained and difficulties in its application are to be avoided, the cases must be recognized and treated early, preferably with the guidance of someone thoroughly conversant with bacteriology and immunity.

E. G. D. MURRAY

## PURPURA

PURPURA may be shortly defined as the extravasation of blood into the skin. In the severer forms bleeding also occurs into the serous membranes and from mucous surfaces. Accordingly, the use of the term "purpura" has been extended to cover these cases as well. The appearance of purpura is always a spectacular event, arousing anxiety, and calling for, in large measure, the resources of diagnosis and treatment. Interest in the subject has recently been accentuated because of the recording of a considerable number of cases following the exhibition of drugs, notably certain of the hypnotic group, and the apparent cure of a particular type of purpura by splenectomy or tying the splenic artery. It will, therefore, not be out of place to review the matter anew.

It will facilitate our understanding of the subject if we realize at the outset that purpura is a *symptom* and not a disease, and that it assumes several forms and is due to many causes. Purpura may manifest itself as the earliest and the predominating physical sign of disturbance; it is then itself the cardinal feature. This form is known as *primary, essential, or idiopathic purpura*. The last two names are not appropriate, as the etiology of this form of purpura is in most cases fairly plain. Again, purpura may be simply an incident or complication in the course of some well-known disease or con-

dition. Then it is called *secondary or symptomatic purpura*. This is seen typically, for example, in typhus fever, in hæmorrhagic small-pox and in poisoning with certain drugs. A classification that seems to have some popularity at the present time is that into *thrombocytopenic* and *non-thrombocytopenic purpura*. This is, in my opinion, objectionable, for the reason that there is no necessary association between the thrombocytes and hæmorrhage through the vessel walls. Purpura may occur without thrombocytopenia and, conversely, thrombocytopenia, without purpura. A classification is indefensible if it is based on one only of a number of factors, and, moreover, one that is inconstant. The number and character of the platelets may vary in different cases and at different times in the same case. We therefore prefer the following, based on an older classification, admitting at the same time that it is not perfect.

### I. Primary Purpura:

- (a) Hæmorrhagic purpura (Werlhof's disease);
- (b) Purpura with arthritis (Schönlein's disease);
- (c) Purpura with colic (Henoch's disease);
- (d) Scurvy;
- (e) Hæmophilia;
- (f) Certain food poisonings.

## II. Secondary Purpura:

- (a) Infectious, as in certain specific fevers, *e.g.*, typhus, cerebrospinal, small-pox, measles, scarlatina, typhoid, sepsis.
- (b) In severe blood diseases, *e.g.*, leukaemia, pernicious anaemia.
- (c) Toxic, as from snake-bite, and poisoning from drugs and chemical substances, *e.g.*, benzene, mercury, iodides, quinine, belladonna, copaiba, ergot, and the constituents of the bile.
- (d) Cachectic; seen sometimes in cancer, tuberculosis, nephritis, and old age.
- (e) Neurotrophic; as in locomotor ataxia, peripheral neuritis, fright, and hysteria (*e.g.*, "stigmata").
- (f) Mechanical; as in venous stasis from paroxysmal coughing, convulsions, and tight bandaging.

Here the term "hæmorrhagic" purpura is, possibly, objectionable on the ground that it is tautological, for every purpura must be "hæmorrhagic," but it is so commonly used for a particular type that it is accepted here. For the rest, it is admitted that the various sub-groups overlap to some extent, but nevertheless they indicate useful generalizations. To illustrate, the infectious purpuras are, no doubt, toxic as well, and the cachectic purpuras are largely toxic. Still, the classification adopted is comprehensive, didactic, and convenient.

On studying the literature dealing with purpura one is struck with the amount of attention that is given to the various alterations in the quality of the blood—in particular, deficient fibrin-formation and diminution in the number of the platelets. Less is said about the erythrocytes and their oxygen-carrying capacity, and less still about alterations in the quality of the plasma. All that is of value in helping us to understand why bleeding does not cease promptly, but still leaves us with the question as to why extravasation of blood through the capillary vessels occurs in the first place. It is, we think, clear that the factors mentioned do not tell the whole story, for they are inconstant and relatively variable. For example, in some cases of hæmophilia and at certain times in obstructive jaundice there may be prolongation of fibrin formation without prolongation of the bleeding time;

in some cases of essential thrombocytopenia the number of the platelets during the remissions may be as low as, or even lower than, it is during the exacerbations when purpura becomes manifest, and there is only slight increase in the bleeding-time; again, it may happen that in scurvy and the Schönlein and Henoch purpuras no abnormality in the blood can be detected, either microscopically, physically, or clinically. There must be, therefore, still another factor—the capillary wall. This is constant, relatively, at least.

In estimating the influence of the vessels in the production of purpura we should remember that the all-important element is the capillary network; the larger vessels, with their thick walls, are merely conducting tubes. The transudation of plasma from the capillaries into the surrounding tissues, necessary for nutrition and metabolism, to be conducted normally, implies that the blood, on the one hand, must be normally constituted and must not contain deleterious substances, and, on the other, that the capillary wall must be vitally unimpaired. Each is the complement of the other. This relationship may be disturbed in many ways. The blood may be disturbed in its cellular elements, in the quality of its plasma, may contain bacteria or other foreign elements, and may carry toxic substances in solution; it may be deficient in nutritive elements, including oxygen. The capillaries may be traumatized, over-distended, and their endothelial cells degenerated. According to circumstances, and under abnormal conditions, we may get oedema, where the plasma transuded from the capillaries is held too long in the tissues; urticaria (including angioneurotic oedema) in which, with the oedema there is congestion; and purpura, in which condition the red corpuscles pass out as well. It would seem that the controlling factor in all this is some alteration in the capillary walls which renders them unduly permeable to the elements of the blood. Conditions that come into mind here are over-distention of the lumina of the capillaries (as in congestion and stasis); changes in the elasticity of the capillary wall; disturbance of the normal contractility (of nervous origin); hyaline and fatty degeneration of the endothelial cells, the result of inflammation, toxæmia, lack of



nutrition; and alteration in the cement substance binding the cells together. Lietermeister thought that the vessels, like the organs, were apt to suffer severe parenchymatous degeneration, which in combination with some blood dyscrasia was an exciting cause of blood extravasation. The older pathologists used to speak of hæmorrhage *per diapedesin* and hæmorrhage *per rhexin*. It seems hard to believe that the red cells of the blood can pass through the substance of the capillary walls, though the white corpuscles, in virtue of their amœboid powers, may do so, as in inflammation. Much more likely that when they do so there is an actual rupture of the capillary. This state of things could be brought about by various factors, either singly or combined, such as, over-distension, actual trauma, inflammation, and degenerations of the endothelial cells. In regard to the last-mentioned, we satisfied ourselves, years ago, that in the secondary purpura occasionally found in typhoid fever there is a fatty degeneration of the capillary walls<sup>1</sup>. The degenerations referred to may be due to lack of nutrition, as in anæmia, anoxæmia, stasis, and avitaminosis, as in scurvy; to pressure, internal

or external; to inflammation; to circulating toxic substances, such as bacterial toxins, snake venoms, and certain drugs and chemicals. Among the drugs that can, on occasion, produce purpura we can mention ergot, quinine, iodides, belladonna, anilin, benzene, copaiba, phosphorus, acetphenetidin, arsphenamin, derivatives of urea, and salicylic acid. Some of these act directly, but others, like anilin, the benzene derivatives, and quinine, indirectly, by damaging the bone marrow. It should be noted here, also, that while some of these agents may manifest an immediate toxic effect, others seem to act more slowly by inducing an allergic state. They are "allergotoxic." This production of allergy leading to a so-called "hæmorrhagic diathesis" is not, however, to be regarded as a property of drugs only; it may be due to certain foods, notably, milk<sup>2</sup>. In the "anaphylactoid" category are now grouped Schönlein's purpura, Henoch's purpura,<sup>3,4</sup> and the Osler erythema group of skin lesions with visceral manifestations<sup>5</sup>.

A.G.N.

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## Editorial Comments

### The Osler Scholarship

In 1932 Dr. G. T. Evans was awarded one of the two scholarships given by the Board of Management of the Montreal General Hospital and Mr. J. W. McConnell, of Montreal, in memory of Sir William Osler. Dr. Evans has since been devoting himself to research work and we have now received the fruits of his labours in the form of a thesis, submitted in partial fulfilment of the requirements for the Degree of Master of Science (in the Department of Experimental Medicine and Surgery), McGill University, Montreal. Unfortunately we can do no more than give notice of this paper as it is too long for publication but we hope that Dr. Evans will find it possible to have it published later on.

Dr. Evans has taken up the problem of the storage and supply of glycogen in heart muscle, because it has seemed to him that it occupies a

more important rôle in the function of the muscle than has been so far realized. To quote from his thesis:

"With the newer knowledge of the chemistry of muscular contraction, carbohydrate has been put in a place of secondary importance, as far as normal physiology is concerned. But when oxygen supply to a muscle is decreased this same newer knowledge points more strongly than ever to the importance of glycogen breakdown for the continued action of the muscle. Anoxæmia of the heart muscle is undoubtedly present in many clinical forms of cardiac failure. Pneumonia, diphtheria, sudden death at high altitudes furnish excellent examples of the possible importance of anoxæmia and therefore of carbohydrate to continued cardiac action. In arteriosclerotic and valvular heart disease the heart undoubtedly shares the general anoxæmia of the decompensated phases, not to mention that primarily occurring cardiac anoxæmia may be at the root of the decompensation. It would not be hard to give many more examples."

He goes on to defend his attitude of trying to extract practical results from an investigation that some might think belonged entirely to so-

called "pure science". In our opinion he is perfectly right in looking upon the specialized fields of experimental medicine or pathological physiology, as a link between the practical, as found in clinical problems, and the purely physiological. After all, where is the dividing line? One may deprecate the pursuit of knowledge only for practical results, for there is nothing which is apt, more effectively, to disturb the judgment and narrow the imagination, but he must indeed be dispassionate who cannot feel the additional pleasure and stimulus that comes from seeing the application in practice of what was sought after only in theory.

We hope that Dr. Evans will be later able to extract from his very careful and detailed experiments material for a conveniently sized paper for our *Journal*. In the meantime we feel that his choice as one of the first recipients of an Osler scholarship, has been fully justified.

#### The Possible Effect of Group Hospitalization on Hospital Construction

The subject of Group Hospitalization, or the Periodic Payment Plan for the Purchase of Hospital Care, as it is sometimes called, is becoming of increasing interest to hospitals, as more and more institutions are adopting, and apparently with success, this method of minimizing the burden of the cost of hospital care to the patient of moderate means. This movement has spread very rapidly in the United States, and for many years has been practised in various parts of Canada. The number of hospitals in Canada developing this plan has increased quite rapidly during the past two or three years, recent additions to the ranks being the public hospitals in Edmonton, and, still more recently, the two hospitals in Kingston.

The effect of the adoption of this voluntary insurance plan will be felt in many ways. One may be the effect on future construction, and this is of importance to hospitals at the present time for a number of them, having delayed construction for a number of lean years, are finding expansion quite imperative, and now,

with the first glimmer of returning prosperity, are seriously considering expansion so as to take advantage of the still unusually low cost of construction. Most group-hospitalization plans provide for the subscriber a set period of hospital care per annum. In most plans the free hospitalization offer is on a public ward basis, but in some semi-private accommodation is specified and, in others, private. Where a contract provides public ward accommodation gratis, it is customary to permit the patient to select more private accommodation by simply paying the difference in the rates. However, it is to be anticipated that with the wider adoption of such plans—and the movement is steadily gaining momentum—the accommodation most in demand in any community will be that provided in the group hospitalization contract of the local hospitals.

Thus one can readily foresee that in some communities, as experience has already indicated, the big demand would be for public ward accommodation, probably four- to six-bed cubicles or rooms, while in others two-bed semi-private accommodation, or perhaps cheap private accommodation, might be in most demand. Few hospitals have accommodation so elastic that services can be transformed without much expense. When the Workmen's Compensation Board in certain provinces required that their patients be given semi-private accommodation, or at least kept separate from the usual public ward, hospitals were put to considerable inconvenience and expense in trying to remodel the accommodation, set up temporary partitions, and otherwise try to meet the request. It may not be possible for building committees to fully anticipate the hospital evolution of the next two decades, but certainly the possible development of group-hospitalization in their communities, whether rural or urban, must be given serious consideration, and any new construction should be of such a nature that it could be readily converted from semi-public to semi-private or private, or *vice versa*, at minimum expense.

HARVEY AGNEW

Lastly, if length of Days be thy Portion, make it not thy Expectation. Reckon not upon long Life: think every day the last, and live always beyond thy account. He that so often surviveth his Expectation lives many Lives, and will scarce complain of the shortness of his days. Time past is gone like a Shadow; make time to

come present. Approximate thy latter times by present Apprehensions of them: be like a neighbour unto the Grave, and think there is but little to come. And, since there is something of us that will still live on, join both lives together, and live in one but for the other—Sir Thomas Browne.

## Retrospect

### THE TREATMENT OF SYPHILIS OF THE NERVOUS SYSTEM\*

BY G. N. PATERSON-SMYTH, M.D.,

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This brief treatment of a most engrossing and important topic consists in the main of a review of Buckley Sharp's recent publication "Neurological Effects of Syphilis", together with a few comments based on experience gained in the Neurosyphilitic Clinic of the Montreal General Hospital.

It is a customary division, and one based on sound clinical, therapeutic and pathological grounds, to separate syphilis of the nervous system into two distinct groups:—

- |                      |                            |
|----------------------|----------------------------|
| 1. Interstitial      | Meningeal                  |
| (cerebrospinal lues) | Vascular                   |
| 2 Parenchymatous     | a. Tabes                   |
|                      | b. Tabo-paresis            |
|                      | c. General paresis (G.P.I) |

The treatment of these two groups varies considerably and the distinction is one that must be kept clearly in mind.

Before launching out into a discussion of treatment it is imperative to discuss preventive measures. The early involvement of the nervous system in the primary and secondary stages is, at times, not fully recognized. In the late primary stage, changes in the cerebrospinal fluid are found in 20 to 30 per cent (pleocytosis, increased globulin), while in the secondary stage, when the blood Wassermann test has become positive, 10 per cent show a positive Wassermann in the spinal fluid, and 66 per cent show an increased cellular and globulin content. One can hardly fail to be impressed by such figures and realize the importance of early and adequate treatment.

#### PREVENTION

Prevention of neurosyphilis means early and adequate treatment of somatic syphilis. The ideal is, of course, to abort the disease while still localized. Every suspicious sore must be examined thoroughly for treponemata, and if any organisms are detected immediate and thorough treatment must be instituted. There is no absolute criterion as to when infection may be considered generalized; obviously it is so when the blood Wassermann test becomes positive, but is probably the case earlier. Sharp suggests that lymphadenitis may be taken as a fair index

of generalization. If the blood Wassermann test is positive, or if secondary signs have appeared, then treatment, while equally energetic, must be even more prolonged. In those cases which remain Wassermann-fast after full treatment a course of treatment should be given once a year indefinitely, *assuming that the cerebrospinal fluid remains normal*. If the cerebrospinal fluid shows some abnormality after treatment then some special form of attack must be utilized (referred to later). Lees advises a check on the cerebrospinal fluid at one and three years after treatment if there is no evidence of neurosyphilis.

Such a régime would seem almost beyond dispute, but there is a certain amount of clinical basis for criticism. It has been suggested that the rapid abortion of early syphilitic lesions tends to lessen the immunity response that goes a long way to protect the nervous system. Bruusgaard, of Oslo, followed up 2,181 cases of untreated primary and secondary syphilis and could find but 13 cases of general paresis of the insane (0.6 per cent), considerably below the normal expectation. These figures vary greatly from those of Mat-tauscheck and Pilez, who, examining a series of 4,134 syphilitic army officers, found 4.7 per cent with general paresis of the insane. These two series are both in the period before salvarsan was known. More recently Lees, in Edinburgh, in a check-up of 13,199 cases of syphilis found 603 neurosyphilitics, giving an incidence of 4.5 per cent. Bruusgaard's deduction that the incidence of general paresis of the insane in untreated syphilis was less than that in treated cases has been proved to be erroneous by a great mass of figures from recent observers, who all, without exception, show that *adequate* early treatment greatly decreases the incidence of neurosyphilis. The crux is that early treatment must be adequate. There is however, considerable evidence to show that *inadequate* treatment is worse than none and tends to precipitate infection to the nervous system. It must be remembered too that cases do occur with a negative blood Wassermann test, but with the cerebrospinal fluid Wassermann-positive.

This naturally leads to a consideration of what constitutes adequate treatment of early syphilis. The answer to this question is rendered extremely difficult by the absence of an infallible test for cure. Warthin has published a series of cases showing post-mortem evidence of syphilis with negative Wassermann tests and feels that this test is of little value in excluding latent syphilis. The Kahn test, more sensitive, has shown a larger series of false positives. The same is true of cases

\* Read before the Psychiatric Section, Montreal Medico-Chirurgical Society, October 17, 1933.



under treatment where the Wassermann becomes negative before the Kahn. It seems advisable to suggest then that both tests be used concurrently. There has been much discussion about false positive Wassermans, but the conclusion now seems justified that, excluding yaws, leprosy and rat-bite fever, a positive Wassermann test, repeated if necessary, may be taken as indicative of syphilitic infection.

In the absence of absolute serological tests for cure, formulation of a scheme of adequate treatment can only be based on experience and follow-up. Under such circumstances it is obvious that there will be little agreement between different authorities. However, Tytler Burke give some findings for sero-negative primary cases: (1) six weekly injections of "stabilarsan", totally 3.45 g., followed immediately by (2) eight biweekly injections of "bivatol" (liposoluble bismuth). This course of stabilarsan is repeated twice, with a bismuth course between. An analysis of 136 cases observed for periods of three months to five years has shown no case of clinical or serological recurrence.

In congenital syphilis preventive treatment must be started in the prenatal stage, for at birth syphilis is long past the primary stage. The treatment of a pregnant woman with lues must be started as early as possible, regardless of her serological state. If adequately carried out up to confinement an uninfected child is practically certain. After antenatal treatment, a child tested at one month and at one year, with both tests proving negative, can be considered healthy. In all cases the cerebrospinal fluid should be checked before and after treatment.

#### TREATMENT

The indication for the adoption of special modes of treatment is, of course, the persistence of pathological changes in the cerebrospinal fluid. Even with negative serological tests, a pleocytosis which persists after adequate early treatment is a clear indication for the initiation of special procedures. In a consideration of the treatment of neurosyphilis it must always be kept in mind that there are two totally distinct types of syphilitic involvement of the nervous system, each type demanding a very different method of treatment:—

*Meningo-vascular* (cerebrospinal) *lues*—included in this group of syphilitic sub-maladies (as Hughlings Jackson puts it), affecting mainly the interstitial tissues, ranging all the way from the meningitides, acute and chronic, and gummata, to the vascular accidents, hæmorrhage and thrombosis. In this type the nervous tissues themselves are not involved. They are therefore amenable to treatment with the ordinary arsenical compounds, (neosalvarsan, etc.) and bismuth. Some authorities (Harrison

and C. P. Symonds) advocate the use of potassium iodide in large doses, though others feel the last is of little value. Solomon and Epstein in Boston advocate the use of tryparsamide (a preparation more fully discussed later), and state that clinical improvement can be noted in three to four weeks and that serological cure is inevitable in the course of a few months. Rudolf has employed malaria in two hemiplegies not improved by routine treatment, with apparently marked improvement, but there are few data on the use of malaria in this type of case.

*Parenchymatous neurosyphilis*.—Tabes; taboparesis; paresis (G.P.I.).—Here the problem of treatment is very different and much more complex. Routine arsenical treatment is useless, since the ordinary arsenic and bismuth preparations fail to diffuse through the choroid plexus, as they must do if they are to reach the affected nervous tissue. This necessitates, then, the introduction of special methods. It will lend clarity to the situation to consider the treatment of paresis and that of tabes separately.

*General paresis of the insane*.—There are three main types of treatment: with malaria; with tryparsamide; with intracisternal salvarsanized serum.

The malaria method, introduced by Wagner-Jauregg, of Vienna, is now being widely used with, on the whole, most gratifying results. The benign tertian strain is generally employed, and the patient infected by the intravenous injection of 2 c.c. of blood from another infected patient. The incubation period is about nine to sixteen days. As a general rule twelve to fourteen bouts of fever, reaching to 104° or higher, are permitted before terminating the course with quinine. Radical though this method must appear, it is justified by the severity of the disease so treated. It is difficult to evaluate the mortality figures because of deaths due to intercurrent infection and those due to the disease itself. The figures from numerous sources would appear to indicate 10 per cent as a fair figure for the deaths due to malaria itself. It is therefore imperative that the prospective candidate for malaria be most carefully examined, more particularly as regards his cardio-renal systems.

During treatment the most careful supervision must be exercised and the treatment terminated at the first unfavourable sign, *e.g.*, jaundice, cyanosis, tachycardia. Nichol stresses the importance of repeated examinations of blood films and states that if, using a one-twelfth oil-immersion lens and a No. 2 eye-piece, thirty-five or more parasites are found in each of 25 fields it is an indication for stopping treatment. If some unfavourable sign appears during treatment, a single five-grain dose of quinine will stop the attack for ten to twenty days without losing the malarial strain. To finally terminate the treatment, Sharpe suggests quinine bismuth hydro-

chloride, grains five, twice daily for fifteen days. In the Montreal General Hospital excellent results have been obtained by much larger doses—gr. vii ss. intravenously, followed by gr. v three times daily for ten to fifteen days. Sharpe points out that quinine will not abort malaria in the presence of an intercurrent infection. Should such a situation arise, the drug of choice is plasmoquine, which, recent work has shown, is lethal to sporozoites and therefore can prevent the development of malaria after infection has set in. In certain cases which are resistant to malaria the injection of T.A.B. vaccine (25 million) intravenously will often evoke a malaria-like paroxysm.

In untreated cases of general paresis of the insane spontaneous remission occurs in about 10 per cent; this remission lasts from six months to three years. The average duration of life in the untreated case is three years.

After malaria Carrière gives the following figures on 579 cases:—

Cured .....	18.83	} 40.59
Fit for work .....	21.76	
Improved (not fit for work) ....	13.47	
No change .....	28.32	} 17.62
Died during treatment .....	1.9	
Died after treatment .....	15.72	

The mode of action of malaria is little understood. The consensus attributes the beneficial results mainly to the fever, secondarily to some obscure specific effect. Serologically the patients show marked improvement, though rarely does the spinal fluid become completely normal. There is general agreement that there is marked histological improvement in the brains of paretics after treatment. During the course of the malaria the inflammatory changes are exaggerated, which increases the permeability of the choroid plexes. On this basis the administration of a course of tryparsamide (8-12 injections) subsequent to the malaria is likely to prove of much value.

Numerous other methods of pyro-therapy have been advocated. In general it may be said that none have yielded results in any way comparable to those obtained with malaria. Recently Schroeder has introduced a suspension of sulphur in oil known as "Sulfosin Leo" which he claims has produced excellent results, but other observers have not confirmed his findings. The most important of these alternative methods is diathermy. The data at present are inadequate to form a considered judgment, but very conflicting results have been reported. The expense of installation and the technical difficulties are severe handicaps to this procedure.

Tryparsamide, a drug originally designed for the treatment of trypanosomiasis, has come much into vogue in the treatment of parenchymatous and indeed all forms of neurosyphilis. In the hands of all observers it has yielded strikingly encouraging results, and is undoubtedly a very

powerful addition to the array of antiluetic remedies. There is the additional advantage of the absence of toxic symptoms. Only one complication is to be feared—optic atrophy. It is unfortunate, perhaps, that the dangers of atrophy have been overstressed. Figures are not readily available; Sharpe quotes 45 per cent, only 1 per cent being permanent. Moreover if frequent ophthalmoscopic examinations are carried out and treatment discontinued at the first evidence of visual impairment recovery is almost invariable. The drug has a high degree of permeability and appears to have an affinity for the parenchyma of the nervous system. The results of various observers are universally encouraging. Stevenson reports 40 per cent good remissions in 35 unselected cases of general paresis of the insane. Tennant, of Maudsley, in a careful analysis of 50 cases, of general paresis of the insane gives the following figures:

Group 1.	Group 2.
Tryparsamide only.	Tryparsamide plus malaria.
18.5 . . . . .	Good remissions . . . . . 47.8
33.3 . . . . .	Moderate " . . . . . 21.7
33.3 . . . . .	No change . . . . . 26.0
14.9 . . . . .	Dead . . . . . 4.5

Every case showed serological improvement though this did not always run parallel with the clinical picture. Further work by Lees and others further enhances the reputation of this drug. These workers stress the general tonic effect, and suggest that it should be reinforced with "914" or bismuth, as the effect of tryparsamide on extra-neural lesions is negligible.

*Tabes* is much more common than general paresis of the insane. In Lees' 372 neurosyphilitics 53.4 per cent were tabetics and but 21 per cent general paresis of the insane.

*Tabes* is a very unsatisfactory disease to treat. The lesions being degenerative, no cure in the line of restoration of function is possible. Some cases in the pre-ataxic stage may be arrested; others show some amelioration of symptoms, but, due to the irregular course of the disease, with its spontaneous arrests and remissions, it is difficult to assess the value of treatment. In general, it seems best to employ the same procedure as in cases of general paresis of the insane. Lees and other workers have obtained excellent results with the use of tryparsamide alone. The results of malarial therapy in *tabes* are conflicting to a degree, but such workers as Wagner-Jauregg and Wullenweber report fair results. It must be remembered that *tabes* is not a progressively fatal disease, like general paresis of the insane; hence the decision to take the inevitable risks associated with malaria must be made with considerable caution.

*Congenital neurosyphilis.*—The congenital group is notoriously recalcitrant to treatment and presents a difficult therapeutic problem.

Infants with positive serological findings



should be given some arsenobenzol compound (Sharp suggests sulfarsenol) which can be given intravenously, commencing with a dose of 1.5 etgm., increased up to 6 etgm. in eight weekly injections. Nabarro, at Great Ormond Street, suggests five such courses separated by a month's rest, increasing the dosage with advancing age up to 12 etgm. Sharp states that if the diagnosis be made early excellent results are obtained. With older children, arsenobenzol can be given intravenously, regulating the dosage by the weight and age. As adjuvants, bismuth and possibly mercury may be given. Excellent results are claimed for a pentavalent arsenical, "stovarsol", which may be given orally, but as yet there are little data upon which to base judgment. Needless to say, repeated check-ups on the blood and cerebrospinal fluid are essential. If after adequate standard treatment of this type the serological tests remain positive, the child is a potential neurosyphilitic and must be treated as such.

The same methods are employed as with adults, tryparsamide is apparently the drug of choice. The results of malarial therapy are very disappointing and only apparently justified in frank juvenile paresis. Nabarro claims some results with intra-cisternal salvarsanized serum, but offers few figures in support. It must be admitted that the prognosis in the congenital neurosyphilitic is uniformly bad.

Sharp summarizes his finding as follows, and suggests the following lines of treatment:—

#### 1. *Cerebrospinal lues*

- (a) Standard treatment with arsenobenzol and bismuth.
- (b) Supplementary treatment with tryparsamide.
- (c) In some cases large doses of sodium iodide intravenously.

#### 2. *General paresis of the insane*

- (a) As soon as diagnosed, tryparsamide.
- (b) Malaria as soon as possible in suitable cases.

- (c) Follow up malaria with tryparsamide and bismuth, with an occasional course of 914.
- (d) Another course of malaria in one to two years if necessary.
- (e) Occasionally intra-cisternal salvarsanized serum.

#### 3. *Tabes*

- (a) Neosalvarsan and bismuth.
- (b) Potassium iodide, oral or intravenous.
- (c) Tryparsamide.
- (d) Malaria in certain selected cases.
- (e) Lumbar injection of salvarsanized serum.

There is little to criticize in the above scheme. It may be said, however, (1) that the emphasis placed on the use of iodide has not been justified in our experience. (2) In the tabetic group tryparsamide has apparently yielded better results than the routine arsenic preparations for the use of which there appears little justification when the process is so definitely parenchymatous. (3) The use of salvarsanized serum, whether by the lumbar or cisternal route, has but little support in the literature, and in view of the difficulties and dangers of the procedure would seem to be justified only in very rare instances.

#### CONCLUSION

An attempt has been made to review briefly the current methods of treatment of syphilis of the nervous system. The implications are obvious, namely, the fundamental importance of adequate treatment in the early primary and secondary stages, and the necessity of early diagnosis when the nervous system has become involved. When these essential truths are fully recognized, then, and not till then, will the present amazingly high incidence of neurosyphilis, with its accompaniments of personal suffering and social and economic loss, be reduced to more reasonable proportions.

The writer desires to express his indebtedness to his chief, Dr. F. H. MacKay, for his kindly criticism and assistance in the preparation of this paper.

QUININE AND ERGOT ALLERGY AND THROMBO-CYTOPENIC PURPURA.—M. M. Peshkin and J. A. Miller report a case in which a definite causal allergic relationship between such drugs as ergot and quinine and thrombocytopenic purpura has been established. Sensitization to drugs inducing various manifestations of allergy has been shown to occur in cases in which such small doses were used as to preclude the possibility of any toxic or even discernible pharmacologic action. Asthma and vasomotor rhinitis have been induced by the inhalation of ipecac, rhubarb, lycopodium and castor bean, and by the ingestion of any of a large list of drugs, including even the synthetic chemicals such as acetylsalicylic acid, phenobarbital, amidopyrine and antipyrine. Other allergic conditions caused by the ingestion of drugs are generalized erythema, urticaria, angioneurotic oedema, abdominal colic and eczema. It has been generally known

that various drugs can cause nonthrombocytopenic purpura and even thrombocytopenic purpura. The patients were regarded as suffering either from an overdose or from the poisonous effect of the drug. It is not generally known that purpura in some of these cases is really due to drug allergy. Quinine is one of the important and useful drugs employed. The authors believe that positive evidence of ergot and quinine allergy in their patient caused by ingestion in the same patient inducing symptoms of thrombocytopenia, with positive skin and passive transfer reactions only to the quinine (levorotatory) group, assumes vast importance, because it carries the inference that drug and other allergenic substances probably enter into the etiology of thrombocytopenia more frequently than the few scattered reports in the literature would indicate.—*J. Am. M. Ass.*, 1934 102.



## Medical Economics

### THE DIFFICULTIES OF THE PROFESSION

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In these trying times many complaints bearing on the economic aspect of the practice of medicine are heard from members of the profession. All complain of the enormous amount of charity work that has to be done, especially in these abnormal times. This applies to work done in hospitals and in homes. In the hospitals the public wards are crowded and the out-door clinics flooded with patients seeking free treatment. The public, generally, still thinks the hospital staff physicians and surgeons are remunerated for their services. Little do they realize that the only compensation lies in the gaining of valuable experience in seeing and treating all kinds of diseases. In general, one may say that members of the various hospital staffs give a good part of each morning to this charity work. This means that the first part of each day, when the body and mind are fresh, is devoted to this work and the rest of the day and night, when mind and body are more and more wearied, is given to those patients who are willing to pay for examination and treatment. This seems hardly fair to the paying part of the laity. Nor is it fair, say the members of these hospital staffs, particularly the younger members, that so much time should be spent in this work and the only compensation be in the direction of experience gained. In no other profession or trade, say they, does a man spend years in equipping himself for his life's work, only to find (when he is sufficiently equipped and considered by our authorities fit to practice) that he must continue to work for little or nothing, to the end that sometime, with good luck, he may be a consultant and get fees for a brief period that may compensate for long tedious years of non-remunerative work. Young surgeons are better off than young physicians, in that they are privileged to attend workmen's compensation cases. One cannot but feel that, valuable as is the experience gained, some monetary return at a reasonable rate should be combined with the reward obtained through a larger experience in the diagnosis and treatment of disease.

The general practitioner during the past few years has felt the hard times almost beyond words. Whether in the country or in the city, many have seen their practices dwindle financially almost to the vanishing point. Plenty of work there has been, but scant re-

muneration. An attempt (to be dealt with in a subsequent article) has been made by our government in Ontario to alleviate the distress of these practitioners. The plan adopted is only temporary, and it would seem that the time is ripe for the practitioners of this province to join hands and demand of the government that some uniform, permanent scheme be brought forward and put in force, relieving and benefiting both doctor and patient, not only in times of abnormal strain but in the so-called days of normalcy.

In many quarters one hears the complaint that we have too many medical organizations, each with its own demands on the resources, financial and otherwise of the profession. The district association, the College of Physicians and Surgeons, the Ontario and Canadian Medical Associations, all make their appeal for help. Does the benefit derived from the services they render compensate for the time and money spent on them? A thousand times—yes, but in Ontario there is a growing feeling that we should consolidate our position, merge the College of Physicians and Surgeons and the Ontario Medical Association into one organization which will carry out the work done at present, without overlapping, with greater efficiency, and with reduced fees. It seems necessary that as a profession in this province we must function as a self-controlled unit if we are to avoid exploitation by federal, provincial and municipal authorities, especially if, and when, health insurance, in some form, comes.

There are, too, difficulties and dangers in the ranks of the profession. These appertain largely to the practice of surgery. One hears complaints frequently from skilful surgeons that many general practitioners are attempting to solve surgical problems for which by training and experience they are quite unfitted. It is admitted by all surgeons that many general practitioners are sufficiently experienced and qualified to deal with the more common surgical diseases that are encountered in general practice. But there are others who, without any justification whatever, attempt the more difficult operations solely for the sake of the monetary compensation, or in lieu of operating themselves refer their patients to one, who without much right, assumes the title of surgeon, and will secretly divide with them the fee obtained for operating on their patients. In some way legitimate surgery must go to those qualified by experience and training in the science and art of this branch of medicine. Again, by some means, secret division of fees must be stopped, as the greed of gain on

the part of those who are parties to this procedure tends to unnecessary operations, and in the case of necessary operations leads to the choice of a surgeon who tacitly admits his inferiority in offering to divide his fee.

Many members of the profession complain that our teaching bodies have been slow in undertaking instruction in physical therapy. This has been remedied in Class "A" universities, but tardiness in starting to teach physical therapy to students has led to a rapid increase in the number of irregulars—osteopaths, chiropractors, etc.—with no inconsiderable patronage from the laity and consequent financial loss to the profession. Most of us will admit this complaint to be well-founded in large part. So useful and impressive did these irregulars make themselves to a large section of the laity that eventually, as a result of Mr. Justice Hodgins' report, they were able to get some recognition from the government and were able to practice as osteopaths and chiropractors, but not with the powers and privileges given our graduates in medicine. As time has gone on they have become more and more insistent that they be placed on an equal footing with the medical profession and this year sees them again before the legislature demanding:

1. The right to serve patients coming under the jurisdiction of the Workmen's Compensation Board.
2. The right to practise in hospitals maintained by the public.
3. The right to sign birth and death certificates.
4. The right to utilize the services of the laboratories of the Provincial Board of Health.
5. The right to be called "Doctor".
6. The right to give anæsthetics and to use anodynes.
7. The right to treat relief cases under the Government's Order-in-Council.

Fortunately, through the activities of the College of Physicians and Surgeons and the Ontario Medical Association, these bills were, one by one, defeated in the last session of this Legislature. But these irregulars will be back again, even in the face of the report of Drs. E. S. Ryerson and F. Etherington after their visit to osteopathic colleges in Kirkville, Des Moines, Philadelphia and Chicago. The final paragraph of this report admirably sums up the situation and our position in regard to irregulars. It reads as follows:

"As a result of our visit to the four osteopathic colleges already mentioned, and after a close inspection of their buildings, plant and equipment, their hospital and clinical facilities, their requirements for admission and length of courses, their curriculum; and, after attending their lectures, laboratory classes and clinics, and after a full discussion with the different members of their faculties and staffs, and, finally, bearing in mind the lack throughout their entire course, of adequate bedside teaching in small groups in hospitals, we are firmly convinced that it would

not be in the interests of the public that the graduates of these Colleges, past or present, be admitted to the Ontario licensure examinations leading to the practice of medicine in Ontario.

As a profession we must leave no stone unturned to see that those admitted into the practice of medicine in this province have the same training (or its equivalent) that we have, premedical and medical, and that they pass through the same portals that we must pass. When they meet these requirements, we feel sure no one in our profession will care what name is thereafter chosen, under which to practice.

In a subsequent paper an attempt will be made to point the way out of the difficulties mentioned in this and the preceding articles.

#### RECENT DEVELOPMENTS IN BRITISH COLUMBIA

The last session of the Legislature will go down in history, no doubt, as a somewhat notable one in Canadian history—indeed in British history. One of the glories, of course, of the political system under which British countries live, is its flexibility and adaptability to the demands of circumstance; nevertheless, many of us must have gasped at the advantage that was taken of this feature by our present government. The Special Powers Act, if it can be made to stick, brings us, one would think, perilously close to a dictatorship—though we believe that it will not be a one-man affair, but government by a small council. One is always sorry to see any tampering, no matter how slight and how well-meant, with the principle on which our parliamentary system is based, namely, control at all times of the executive by the elected representatives of the country; but there is an emergency, and we have elected a government to do certain things, on their promise to do these things. We must, in common fairness, give them every opportunity to make good their promise, and stand behind them while they try to do so.

But this was not the thing about the last session that most immediately concerns us. We have seen the day come at last, in spite of all our efforts to the contrary, when a government, whose duty it is to safeguard health and the lives of its citizens, has yielded to popular clamour, and allowed rights of practice to a body of men who, while we might admit that they are sincere and honest in the claims they make, inasmuch as they believe in the efficacy of their treatment, are yet quite untrained—many of them with no scientific or cultural background.

Over the years this province, like others, has built up an elaborate system of health laws and health measures. Medical Acts have been

framed, designed to protect, not those who claim to practise medicine, but the public, against ill-trained men or charlatans. The standards of medical licensure, of medical training, have grown higher year by year, and the tests more rigid. Health laws dealing with sanitation and epidemiology, school medical work, maternal protective measures—all these have been built up along the most advanced lines. Yet we find the premier of this province defending and endorsing an act which admits men who for many years denied the existence or importance of bacteriology or epidemiology, whose knowledge of the human body, its laws and disease, is minimal, and whose preliminary standards of education and scientific training are sketchy, to practise medicine, in the sense of the healing art. We understand that certain restrictions have been attached to the Act—and it may be that not much harm, and some real good, may be done by these men—but we submit with all due deference that this is a distinct dereliction of duty on the part of those to whom we must entrust the health and safety of our growing children and our families. Nominally, we understand, this is not a government measure, yet the list of names of those voting for it reads almost like a list of the cabinet, and we cannot see how they can escape the responsibility for its passage.

We are glad, however, that the Medical Council saw fit to stay out of it. We believe they did the right thing. We have, and we are proud of it, resisted this letting-down of our educational and health standards for many years—but after all, the protection of the public, which, in spite of our detractors, was

our only object, is the duty and responsibility of the Legislature, and not ours—and we believe it was a wise thing to leave it so.

A third matter of great import is the nearness on our horizon of a Health Insurance measure. Time will not permit us to deal with this now, but the latest developments referred to above make it all the more necessary that we should be on the alert in this regard.—Edit., *Bull. Vancouver Med. Ass.*, 1934, 10: 144.

#### WINNIPEG NOTES

On May 21st the Winnipeg City Council unanimously extended for a further three months the existing agreement with the doctors for furnishing medical relief to the unemployed. The cost for the first ten weeks, starting on February 21st, has been \$15,789.00, all of which the city pays. The Council passed a resolution asking that the Dominion and Provincial governments be advised of these costs and urged to share jointly in this relief. Alderman Andrews, chairman of the Unemployment Committee, reported that on the whole the agreement had worked smoothly. Two hundred and four doctors have participated in the scheme, and the net costs of \$15,789.00 represented the following items: operations, 44½ per cent; house and office calls, 42½ per cent; and maternity, 10 per cent. No doctor received more than \$100.00 a month for relief work done in Greater Winnipeg. So far no increase or decrease in the number of patients admitted to hospitals had taken place as a result of the plan. A formulary has been drawn up in an endeavour to offset the mounting costs of prescriptions.

CARBON MONOXIDE ASPHYXIA has received so much publicity that an increasing number of investigators are offering new methods of treatment. The proposed remedies are mainly respiratory stimulants. The evidence offered for them is that animals asphyxiated to the point of failure of respiration survive if the drug is at that instant administered. Clinically the physician must apply the remedy at almost the exact instant at which respiration fails. If he arrives ten or even five minutes later, the victim will be beyond recovery. Owing to the fact that the respiratory stimulant drugs (such as lobeline or methylthionine chloride) have deleterious effects on the heart and circulation, the patient may be better next day if the drug is not administered. Many physicians fail to understand that asphyxia and failure of respiration are by no means the same, even if the one may lead to the other. A patient comatose from asphyxia, and likely to die some hours later, is often

found breathing with even more than normal vigour. What he needs, and all that he needs, is removal of the carbon monoxide, restoration of the oxygen-transporting power of the blood and replacement of the carbon dioxide that has been lost during the development of asphyxia. None of these steps toward recovery, according to Henderson and Haggard, can be promoted to any considerable degree by any hypodermic medication, but they are all directly achieved by the inhalation of oxygen and from 7 to 10 per cent of carbon dioxide. This treatment is now so well established theoretically, and has saved so many hundreds of lives, that it must still be considered the method of choice. Since the introduction of the inhalational treatment of carbon monoxide asphyxia, the deaths from illuminating gas poisoning in New York City for the six years ended with 1932 have been as follows: 611, 570, 525, 435, 305 and 278. This is a striking demonstration of the effectiveness of this treatment.—*J. Am. M. Ass.*, 1934, 102: 217.



## Notes on the British Pharmacopœia and Canadian Formulary

### Nitrous Oxide in the B.P. and C.F.

The extensive employment of nitrous oxide as an anæsthetic has resulted in the production of a gas of very great purity. In the B.P. of 1932, in addition to tests for purity and identity, regulations are made for sampling the gas to determine the content of nitrous oxide which is set at 93 per cent. In America for a number of years manufacturers have been supplying nitrous oxide to hospitals, anæsthetists and dentists of a purity from 98 to 100 per cent, and in view of the fact that in Canada such nitrous oxide is now being sold, the Editors of the Canadian Formulary deemed it advisable to include a monograph on nitrous oxide, in which the regulations stated were the same as in the B.P. 1932, with the exception that the gas, when analyzed, must show 98 per cent or over of nitrous oxide. Manufacturers and retailers of nitrous oxide in Canada did not resent such a high standard; in fact they welcomed such regulations. The impurity of greatest amount in nitrous oxide is nitrogen. While this is not toxic, and would do no harm to the patient, it would necessitate the use of higher percentages of the gas and therefore less oxygen in the production of anæsthesia. The greater anoxæmia would cause greater danger to the patient. There remains only one manufacturer of nitrous oxide in Canada, The Cheney Chemicals Ltd., and the gas produced in this plant, when analyzed, has met all Canadian Formulary requirements. Nitrous oxide other than that produced by this company is imported from the United States in large 3,200 gallon cylinders; it is pumped from these into smaller tanks which fit the various machines employed for administering nitrous oxide. This gas is of a high standard of purity and is carefully controlled by the manufacturers.

Three points of interest may be considered in respect to nitrous oxide. In the first place, nitrous oxide is almost a water-free gas, the B.P. requirement being 0.002 g. per litre of water vapour. The dryness of this gas assures the operator of a steady flow of gas from the cylinders through the reducing valves, for there is no water to form ice to produce a stoppage of the flow. It is no longer necessary to wrap warm towels about nitrous oxide tanks to prevent freezing when gas is being delivered. Secondly, the dryness of the gas may have some injurious effect in the respiratory passages if there is any premedication with atropine, which decreases bronchial secretion. Thirdly, the anæsthetist or chemist must realize that the nitrous oxide in the cylinders is practically all in liquid form. Each cylinder is filled with liquid to a

certain capacity, and above the liquid will be a gas which, if the nitrous oxide which is being pumped into the cylinder is absolutely pure, will be pure nitrous oxide. If, however, there is a small percentage of nitrogen, since the nitrogen at the pressure of the nitrous oxide is not liquefiable, the nitrogen will collect in the gaseous portion in the upper part of the tank. When one opens the valve with the cylinder in the upright position, only gas escapes and the first gas will contain most of the nitrogen. This is the reason for stating in the B.P., 1932, that in performing analyses for nitrous oxide the gas must be drawn from a cylinder in the upright position. If one were to leave the cylinder on its side, on opening the valve liquid would escape and, immediately volatilizing, would give pure nitrous oxide and lead to an erroneous deduction as to the purity of the contents of the tank.

Tanks or cylinders designed to hold liquefied gases must never be filled beyond capacity; each tank must have a definite gas space above the liquid, the space varying with the individual gas. This gas space must be left, so that if the tanks are exposed to a higher temperature than that at the time of filling the increased pressure due to the expansion of the liquid will lead to a liquefaction of the gas in the space and the pressure will not increase greatly. If the tank were filled over its capacity the expanding liquid would eventually fill it and finally lead to its rupture.

The pressure of a tank of pure nitrous oxide will be constant for a given temperature as long as any liquid nitrous oxide exists in it, and will be the vapour pressure of liquid nitrous oxide for that temperature. The pressure will, however, be increased by any nitrogen present which does not liquefy at the pressure which the nitrous oxide tanks are able to withstand. Consequently, the more nitrogen, the greater the pressure shown by a tank filled to capacity; the pressure will be that of gaseous nitrous oxide and the nitrogen which occupy the space above the liquid. Some years ago, when nitrous oxide contained greater amounts of nitrogen than it does to-day, some anæsthetists were led to believe that when the gauge registered high on a tank, say 1,200 lbs. at 76° F., whereas on another tank it showed 900 lbs., the tank with the higher pressure contained more nitrous oxide. In reality both tanks might contain the same amount of nitrous oxide, but the one with the nitrogen gave the higher pressure. The pressure registered gives no indication of the amount of nitrous oxide in the tank as long as some

liquid is left; it records purity only, and the quantity of gas must be estimated by weighing the cylinder.

The Editors therefore included in the Addendum of the Canadian Formulary a table of pressures which a standard gauge should register at various temperatures when attached to a tank filled to capacity or under with 99.3 per cent nitrous oxide. One must be certain, of course, that the gauge registers correctly. Given an accurate gauge, the table in the Canadian Formulary enables one to estimate the percentage of nitrogen present as an impurity, since for each percentage of nitrogen the pressure increases about 20 lbs.

#### The Local Anæsthetics of the B.P.

The Pharmacopœia has extended its list of local anæsthetics. Novocaine, under the name Procaine Hydrochloride, is at last included. As a synonym, "Ethocaine" is given, but the trade names are many, Syncaine, Allocaine, Kerocaine, Anocaine. The profession may well expect and insist that these trade names be now given up. A dose for administration per os is given. This seems of no value, and the dose for intraspinal administration, "up to 150

mgm.", is very frequently exceeded and is hardly of any value.

Stovaine, under the caption of "Amylocaine," is also included. The use of this local anæsthetic is undesirable, as it has irritant qualities which should lead to its use being discouraged.

Benzocaine, ethyl-amino benzoate, is better known under its other trade name "Anæsthesine." Why "Benzocaine," a known trade name, was employed is not known. Orthocaine is another benzoic acid derivative, commonly called Orthoform, or, better, New Orthoform. Both these are local anæsthetics of the but slightly soluble type, which have been used successfully for painful wounds, ulcers, etc., of the skin, and for accessible mucous membranes. To these they may be applied in the form of dusting powders, or ointments. They have been employed to relieve the pain of gastric ulcer, but this seems to have been neither successful nor advisable.

It must be remembered by critics of the Pharmacopœia that the admission of substances covered by patents presents a great difficulty that can be but rarely overcome, and possibly this has prevented the inclusion of certain of the other local anæsthetics.

V.E.H. AND G.H.W.L.

### Men and Books

#### DR. SOLOMON SECORD

In the town of Kincardine, Ont., near the post-office, stands a monument to Dr. Solomon Secord. The present year, 1934, is the hundredth since the birth of this notable man. Why this monument was erected we can learn from a lecture by Mr. Orville Taylor, which is here in part reproduced from the *Kincardine Review* of March 15, 1934.

This year of 1934 is the one hundredth anniversary of the birth of Solomon Secord, a member of the same family that gave us Laura Secord in an older generation. His birth-place was near Burlington Bay and as he grew up he chose medicine as his profession. While still a young man, in the late fifties, he went to Bruce County, first to Walkerton, then to Kincardine.

Evidently Dr. Secord shared that spark of courage and adventure that we associate with the story of Laura Secord. We find him going down to Georgia, when first the United States began to be convulsed over the question of state rights and slavery. It is said that no one expected war to result, except Dr. Secord's father. The young man was sure the trouble would blow over, but he was evidently drawn to the centre of the trouble at a crucial moment in history. An ardent abolitionist, he was as outspoken as his generation knew how to be

and such expression was mighty dangerous in a southern state with feeling running high. His arrest followed, and probably no man had a more narrow escape from hanging. His trial was as irregular as trials were apt to be in those disorganized days when every district made and enforced its own laws, if so orderly a word as law can be applied to the disorderly and hysterical rule of a disrupted people. However, Dr. Secord had friends in Georgia, as he had friends everywhere throughout life, and they intervened.

Now we see the fine spirit of the man. Though an abolitionist he was found in the south, and the men of the southern army were suffering and their need was as great as though they had been on his side of the argument. So we find him enrolled as surgeon in the 20th Georgia Regiment and serving with them throughout the war. He was captured by the northern army and held as a hostage for several months at Fort McHenry, near Baltimore. Perhaps his captors did not know the Secord spirit and the story of 1812. Secord, with some comrades, scaled the walls and escaped. In New York, friends rallied around and helped him to go back to his work with the southern army, where he remained in charge of hospitals, with the rank of surgeon-major.

In Kincardine he married, brought up his



family, and became a perfect example of the old-time family doctor. In 1910 he died at the age of 76, still in harness, though failing health had been his lot for years. The story of his funeral still survives and tells of a whole countryside mourning the passing of a beloved friend.

What was the peculiar quality of this man that he should be singled out for honour in a community that had its share of brave pioneers? Surely it was the spirit that has made so many districts keep green the memory of a doctor.

We cannot better see the beloved Doctor than



through the memories of his friends and from them I have gleaned some stories that show what manner of man this was. We find that even as far back as 1882 Dr. Secord did not go alone on his long drives about the country, for he had a heart condition that made it dangerous. One of the companions who shared many a long cold drive about the country has cherished memories of incidents that show the jolly, friendly doctor as his friends and patients saw him. There is, for instance, the story of a Christmas Day when he had to go many miles to attend a patient who was seriously ill. Finally he was free to leave and his dinner was waiting at home. The people of the house urged him to stay and share their dinner, hot on the table and most enticing. But no, he could not disappoint his own folk. So he took a leg of the turkey for himself and his friend

and off they set on the long drive home to the belated dinner that was so often the portion of the busy country doctor.

Another story tells of the anxious inquiry of a husband as the doctor left the bedside of his wife: "What do you think of my wife today, Doctor?" Said the Doctor, "Oh, she is a mighty fine woman." And with that he jumped into his buggy and was off. So he covered his emotion and his sorrow for a friend for whom he feared a grievous loss.

There is also the story told so often of those brave old family doctors in the days when diphtheria was a plague that must be endured. A child lay ill unto death and Dr. Secord, after lancing the throat, sucked the vile infection with his own lips. The number of boys named Secord throughout the district gives some idea of the number of parents who felt they must pay the highest compliment in their power to the man who meant so much to them. One such Secord was the son of a man who nearly died of typhoid fever and would have died indeed if Dr. Secord had not made daily trips over rough roads for six weeks, though he knew all his pay would be the gratitude of a family and the satisfaction of saving a father whose children needed him. Then there was the woman who had a girl in high school, an adopted daughter, adored by this woman who had made the child her own. The girl became very ill and the mother could not afford the dainties needed. So quietly and unobtrusively the doctor would slip in with food from his own home. Simple stories in a way, but all worth-while stories of real life are essentially simple. They paint for us the picture of a man of courage, with a tender heart, a man probably possessing a bit of a temper and capable of risking his life to right a wrong; a physician with the highest ideals and full of zeal in his chosen work as the servant of the sick and afflicted. There were many such among the old country doctors of an earlier day.

DR. WELCH

BY W. W. FRANCIS, M.D.,

Montreal

The villagers of Norfolk, Connecticut, usually reach their nineties, but in the Welch family, which in four generations supplied some ten doctors to the community, to the neighbourhood, and (the last one) to the world, the traditional age for dying is the early eighties. In front of the house in which William Henry Welch was born in 1850 there is a memorial to his father—locally the greatest of the dynasty—in the form of a fountain for thirsty horses. *Fons sum solati, talis et ipse fuit*, is the inscription it bears. *Qualis pater, talis filius*—such, too, was the son



whose ashes were laid to rest with his kindred in the eighteenth century "burial-yard" on May 4th.\*

Welch graduated in arts at Yale in 1870 and in medicine at the College of Physicians and Surgeons of New York (Columbia) in 1874. His medical course was interrupted by two most significant years, "wasted", according to his friends, one in teaching Greek and Latin, the other in taking a course in chemistry under two teachers who inspired him with the scientific spirit. After an internship at Bellevue he spent two years in Europe, chiefly in Germany, studying histology and pathology under Waldeyer, Cohnheim and other famous teachers. At Breslau under Cohnheim, whom he always revered as his master, he made his first important contribution, an experimental study of oedema of the lungs. In London, on his way home, he was much impressed by the work of Lister. Returning to New York in 1878, he taught anatomy and pathology, eking out a bare living by practice and by conducting "quiz" classes. He soon succeeded in getting a couple of small rooms at Bellevue Hospital for a pathological laboratory, the first in the United States. This he gratefully and gracefully refused to leave when his own school, the College of Physicians and Surgeons, woke up and offered him better accommodation. In 1884 began the connection with Johns Hopkins which ended only with his death, 50 years later, on April 30th last. He inaugurated it with another year abroad, this time studying the new bacteriology under Flügge and Koch. From 1885 until the Hospital was opened in 1889 Welch and his laboratory constituted the entire medical department of Johns Hopkins University, training such famous pupils as Councilman, Mall, Nuttall and Abbott. He and Billings chose Osler, Halsted and Kelly in 1889 and, when the Medical School was organized in 1893, it was Welch who was responsible for the unheard-of scientific and linguistic requirements for admission. As Osler remarked to him, "It is lucky you and I get in as professors; we would never get in as students!" At the age of 66 he resigned the chair of pathology to organize the School of Hygiene and, as if that were not enough, at 76 he began to build up the Institute of the History of Medicine, also the first of its kind in America. He had the satisfaction of leaving this completed and in most competent hands. The beautiful building housing it and the library, which he largely collected in his last years and which bears his name, is his visible monument. Teacher and investigator until 40, during the second half of his life he was teacher, administrator, and servant of the public in all that relates to health. What Osler did for ward

teaching he did, and more, for the laboratory. Between them they wrought a fundamental reconstruction of medical education in America. Much of Welch's influence was exerted, always unobtrusively, through the Rockefeller Institute, of which he was nominally president of the board of scientific directors and really the soul. His public services were handsomely recognized in the great national celebration of his 80th birthday.

The words he applied to Osler apply equally to him, "He belonged to that small but attractive group of physicians, represented in all ages, who combined the broadest humanism with the best science of their day." There cannot often have been two such, working together in the same school. "For a young man the privilege of browsing in a large and varied library is the best introduction to a general education." Thus Osler, with reference to his own two years in Bovell's house; and Welch who, according to Osler, had "in addition to a four-storey intellect, a well-stocked attic", attributed that stock of erudition largely to the fact that in his New York days he was entrusted with a key to the city's best library, then open only two hours daily, and spent his evenings there, or rather his nights, for he was always a late worker. It has been said that Welch wrote little, but this is confuted by the three large volumes of his "Papers and Addresses", collected and published in 1920 in honour of his 70th birthday, though it had to be confessed that many of the addresses were printed from stenographic reports. He could speak extemporaneously, and supremely well, on almost any subject, and on formal occasions, such as demand a manuscript, has been known to produce an irrelevant one and pretend to be reading from it. The Rockefeller Institute had to wait two years for his promised introduction to their edition of Billroth's "Medical Sciences", 1924. Mr. X told me how he finally obtained it by means of a how-about-it postscript to a letter saying that the Foundation was considering his request for the endowment of one of his pet schemes. When later I mentioned X's postscript to Dr. Welch, he cut me short with a chuckle, "Did he tell you that that five-page introduction is the most highly remunerated work in the whole history of literary composition? They had to pay me a million dollars for it!"

Welch adroitly combined dignity with shortness and rotundity, and even with a ridiculous nickname, which, however, connoted nothing but filial affection. Despite Osler's impish allegations that "Popsy" was not really a bachelor, his innumerable children are all of the spirit. His personal finances he left entirely to the care of those who understood them—until he was 83, when he anxiously enquired whether there would be enough for his old age, and was naively surprised and delighted to learn that he was well

\* Read "The doctors Welch of Norfolk", by Harvey Cushing, *New Eng. J. of Med.*, 1934, 210: 1132.

off! Blessed are the meek. His wit and learning, and unerring judgment, were equalled only by his kindness of heart and tongue, by his unfailing courtesy and extraordinary humility. A great teacher, "he dispensed not only knowledge but wisdom."

DE VENARUM OSTIOLIS, 1603, OF  
HIERONYMUS FABRICIUS OF  
AQUAPENDENTE (1533?-1619)

A Review.

By J. H. ELLIOTT,  
Toronto

Students of medicine and of the history of medicine are always grateful to author and publisher when there appears an annotated English translation of a medical classic. To the relatively small but growing number of such translations from the Latin, the latest addition is that most important anatomical treatise, *De Venarum Ostiolis*, published by Fabricius at Padua in 1603.\*

Canano, the Professor of Anatomy at Ferrara in 1545, had told Fabricius of his discovery of valves in the openings of the azygos and renal veins, but did not publish his results. Amatus Lusitanus in his work of 1551 tells of Canano demonstrating these valves, but, erroneously said that the valve opposed the flow of the blood from the azygos into the vena cava. Charles Estienne, in 1545, gave vague descriptions of valves in the liver veins, but it was Fabricius who first demonstrated in his dissections in 1574 the general distribution of the valves of the veins throughout the body, and began public demonstrations of them in 1579. He did not publish his observations until 1603. In the meantime Salomon Alberti, Professor of Anatomy in Wittenberg, published his "*De Valvulis*" in 1585 with the first printed drawings of venous valves, and in this book he acknowledged his indebtedness to Fabricius.

Hieronymus Fabricius was born at Aquapendente near Orvieto about 1533, and began his studies about 1550 at Padua, whose university was then probably the most famous in Italy. His studies in medicine were preceded by Greek and Latin, logic and philosophy. The Chair in Surgery (including anatomy) was then occupied by Gabrielle Falloppio who had succeeded Vesalius when the latter left Padua to see his great *Fabrica* through the press. Fallopius, known as the *Æsculapius* of his age and a great anatomist and teacher, found in Fabricius a young man full of zeal for his

studies in surgery and anatomy, a student gifted with a remarkable memory, a logical and penetrating mind, keen powers of observation, with pleasing manners and an address which marked him out both in public and in private. He was a good demonstrator, and on the death of Fallopius in 1562 gave private lessons in anatomy. Vesalius who for some time had been living in Spain was again offered the Chair of Surgery, but was at that time traveling to Palestine and on his return voyage was shipwrecked and drowned, or died of exposure. In April, 1565, Fabricius was appointed by the Senate to the Chair of Surgery on the understanding that he should teach anatomy also, and for this he was to receive 100 florins a year. Six years later he was reappointed at 200 florins. His second reappointment was in 1577 at 400 florins. In 1584 his third reappointment was made at 600 florins. In 1589 came his fourth reappointment at 850 florins. In 1594 his reappointment carried a salary of 1100 florins. In 1600 he was confirmed in his chair for life with a salary of 1000 scudi, about seven times his former stipend.

In 1609 the Chairs of Surgery and Anatomy were separated by ducal decree and Fabricius remained as Supraordinary in Anatomy alone, with Casserius, named by him, in the post in Surgery. He finally retired in 1613 after fifty years of teaching. He had amassed great wealth, estimated at his death in 1619 at 200,000 ducats, including a large estate a few miles from Padua, where he loved to entertain on a lavish scale; yet he did not give up work, but continued to write, revise and republish up to his last year. Throughout his writings there is evidence of his thorough knowledge of the ancient writers, especially Celsus and Paulus *Ægineta*. A careful surgeon, he wasted no blood in his operations; he ligated arteries, gave directions for tracheotomy and thoracentesis and the surgery of the urethra. He advanced orthopædic work by devising fixation for the neck and means for overcoming vertebral deformities. His services were sought throughout Italy and he had a large practice among the well-to-do. Only an indefatigable worker could accomplish what he did in teaching, research, publication and practice. He not only made a great name for himself and added much of value in medical science, but he stimulated his students, so that his influence spread far and wide. He made the medical school at Padua famous. In one hundred years, which included his fifty years of teaching, 10,000 students passed through the medical school, and many of these became teachers in Padua and other cities throughout Europe.

Among the students was William Harvey, who came to Padua in 1600 and received his M.D. in 1602, the year preceding Fabricius' publication of *De Venarum Ostiolis*. There can

\* *De Venarum Ostiolis*, 1603, of Hieronymus Fabricius of Aquapendente. Facsimile Edition with introduction, translation, and notes by K. J. Franklin, D.M., Tutor and Lecturer in Physiology of Oriel College, Oxford. XII + 98 pages. Price \$3.00. Charles C. Thomas, Springfield and Baltimore, 1933.



be no doubt that Harvey worked with Fabricius in making his dissections, and we learn from Robert Boyle's writings that Harvey told him his work on the circulation of the blood arose from his knowledge of the valves of the veins and his desire to understand their design in nature. *De Venarum Ostiolis* then may be looked upon quite properly as the record of a discovery which, directly or indirectly, stimulated Harvey to observe and experiment, to the end that he gave the world his immortal *De Motu Cordis*, our first great work in experimental physiology.

And now for the first time this monograph of Fabricius, which played such an important part in the history of medicine, is made available in an English translation. The editor, Dr. Franklin, adds to the translation a facsimile of the original made from the copy in the Library of the Royal Society of Medicine; both text and plates are reproduced. There is a short biography of Fabricius, a critical study of the early history of work on the venous valves, a bibliographical note on the first editions of the book, and a list of the references in the text.

The volume should find a place in every medical library, should be available for every student in medicine; and every physician interested in the growth and development of our knowledge of medicine will have pride in the possession of a copy. It has been published by the aid of a grant from the Carnegie Corporation to the History of Science Society, and bears the imprimatur of Prof. G. S. Brett, of the University of Toronto, as Chairman of the Publications Committee of the Society.

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## Hospital Service Department Notes

### Medical Staff Reorganization at the Hamilton General Hospital

Information has been received that the basis of organization of the medical staff of the Hamilton General Hospital has been given considerable revision. This hospital is a large civic institution of some 618 beds, and for the past three years the professional services have been under the direction and supervision of one director-in-chief. Under the new arrangement the medical superintendent will be the official head of the hospital, subject to the Board of Governors and the Advisory Council, and shall have complete control of the surgical, medical and nursing staffs. He shall recommend to the Advisory Council the number of departments

required and the heads of services and their duties. The superintendent, after consultation with the Medical Board, shall submit to the Advisory Council the duties and functions of the Medical Board.

The Advisory Council shall be made up of: a chairman and three members of the Board of Governors; the chairmen of the Medical Board, of the Medical Staff and of the Academy of Medicine; there shall be also two additional members from the Medical Staff and two others from the Academy of Medicine, elected by their respective bodies and without voting powers. The Medical Board shall be composed of the Heads of the various Medical Services, the Superintendent, and the Chairman of the Medical Staff.

This is an interesting way of dealing with the problem of staff organization and control in a large civic hospital, and its progress will be watched with interest. Perhaps its most outstanding feature is the emphasis which it gives to the position of the medical superintendent as the chief executive of the institution. Obviously, this arrangement could be developed only where the superintendent has had a medical background. In the report of the re-organization committee, which was adopted, the rigorous enforcement of the provisions to eliminate any secret division of fees was urged.

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### Roman Catholic Hospitals in Canada

An analysis of the extent of the work done by the Roman Catholic hospitals in Canada and the United States and a review of their schools of nursing have been issued recently by the Catholic Hospital Association of the United States and Canada. Of the 893 hospitals in Canada, 163, or 18.2 per cent, may be properly designated as Catholic hospitals. Of the total bed-capacity of 87,743, 26,704, or 30.4 per cent, are to be found in Catholic hospitals.

These figures indicate a considerable growth, as at the end of 1918 there were but 101 Catholic hospitals in Canada with a total bed-capacity, including bassinets, of 10,999, an increase of 142.8 per cent in 15 years. The average number of beds in each Catholic institution is 163.7; the average capacity of *all* hospitals is 98.2 beds. At the same time 46.5 per cent of the Catholic hospitals are of 75 beds or less. Naturally, the Province of Quebec has the greatest number, with 57 Catholic hospitals; Ontario has 28, and Alberta 23. It is interesting to note that Ontario, with 437 bassinets, leads the Province of Quebec with 342. Hospital facilities reached their greatest density in the ecclesiastical province of St. Boniface, where there is one bed in a Catholic institution for every 58 of the population. The Province of Vancouver is next with 1 in 86. The American College of Surgeons has approved 57

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All communications intended for the Department of Hospital Service of the Canadian Medical Association should be addressed to Dr. Harvey Agnew, 184 College Street, Toronto.



of the 162 Catholic hospitals in Canada. Seven have been approved for internship by the Canadian Medical Association and 5 placed upon the recommended list.

The review of nursing education in Canada indicates that 74 of the 256 training schools in Canada, or 28.8 per cent, are under Catholic auspices. Their pupils represent 36.2 per cent of all student nurses, or 3,388 out of a total student body in Canada of 9,343. Catholic schools, on the average, are larger than non-Catholic schools; the average student census per school for Canada is 38.4, whereas in Catholic schools it is 45.7. It is apparent that the sisters in Canada are taking seriously the appeal to limit the number of students, as there has been a considerable decline in the average student enrolment. The patient-to-student-nurse ratio in Catholic hospitals with training schools is 3.5. This ratio is approximately one-third better for Canada than it is for the United States, where it is 2.7. It is of interest to note that slightly less than one-quarter of all the Catholic schools, namely, those having student census between 50 and 125 student nurses, contain 50 per cent of all student nurses in Catholic institutions.

The percentage of Catholic hospitals affiliated with colleges and universities is higher for the schools of Canada than it is for the schools of the United States; in Canada 41.8 per cent have affiliated with a College or university.

A study of the curricula indicates that the standard in Canada is gratifyingly high and is showing a steady progressive improvement. Entrance requirements are being raised, curricula are being completed, affiliations extended and the instructional staffs increased. An enquiry into the enrolment of non-Catholic students yielded the surprising results, based upon enquiries from two-thirds of the total schools, that the average number of non-Catholics per school is greater than the average number of Catholic students, the non-Catholic students representing 56 per cent of the total.

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THE PREVENTION OF PROSTATISM.—J. F. McCarthy states that it is necessary to have an acute awareness of the advent of prostatism and to remedy the condition by some method such as the cautery punch operation, and thus to obviate the vicissitudes incidental to progressive enlargement of this gland, to enhance the economic usefulness of the patient and ensure serenity of mind to him and his family, when his mental capacity is at its peak and his physical resistance is approaching its inevitable decline. This, it seems to the author, is the problem of the immediate future, not of urologists, but of the medical profession in general, because it is they who first encounter such patients, and the success of this educational campaign depends on their perspicacity and capacity for cooperation.—*J. Am. M. Ass.*, 1932, 99.

## Medical Societies

### The Edmonton Academy of Medicine

The April meeting of the Edmonton Academy of Medicine was of particular interest and importance. Dr. F. H. H. Mewburn gave a practical demonstration on the management of fractures of the phalanges and metacarpals. This was followed by the guest-speaker from Calgary, Dr. E. P. Scarlett. For some years the Calgary and Edmonton societies have once a year had an exchange of speakers. Dr. Scarlett gave an interesting and instructive paper on "The diagnosis and prognosis of heart disease in general practice."

Following this, the question of organizing the profession in the city, and endeavouring to get the cooperation of the men throughout the province in obtaining a uniformity of action, in view of the proposals of the Government to introduce some form of governmental supervision over the practice of medicine was taken up. Much discussion ensued, and a resolution was passed recommending that the College of Physicians and Surgeons and the Alberta Medical Association be asked to bring about a more closely-knit organization which might confer with the government in the making of medical appointments under any contemplated scheme of medical service, and also help to establish the basis for the proper remuneration in accord with services rendered. An appeal was to be made to the Canadian Medical Association to take active steps to secure similar action in other provinces of the Dominion.

In regard to medical services to city relief cases, the Academy adopted the Winnipeg scheme and prepared an agreement to be signed by members who approved this procedure. Only one member failed to agree. A committee was appointed to interview the city council, but no definite action has been taken to date.

Following an annual custom, the Academy was a guest of the Provincial Mental Hospital at Ponoka, seventy miles distant. Dr. Baragar, Dr. G. A. Davidson, and the staff presented a program and illustrated their papers by cases. The program was as follows: Dr. Baragar: "The mental hospital and its work"; Dr. MacLean: "Manic, depressive and involuntal melancholia"; Dr. Cassels: "Schizophrenic reaction types"; Dr. Hamilton: "Mental deficiency"; Dr. MacPherson: "Neurosyphilis"; Dr. Michie: "Senile and arteriosclerotic states"; Dr. Roxborough: "Drug addiction"; Dr. Davidson: "Neurological conditions".

It was of interest to note that outside of Drs. Baragar and Davidson, graduates of the Manitoba Medical School, the other members of the staff received their medical education at the University of Alberta.

HEBER C. JAMIESON

### **The Montreal Physiological Society and the Toronto Physiological and Biochemical Society**

At a joint meeting of the above-mentioned societies held on May 14, 1934, the following papers were read, published here in abstract.

**CHEMICAL STUDIES IN ADDISON'S DISEASE**, by  
J. S. L. Browne and Eleanor M. Venning.

Two patients with Addison's disease were treated with sodium chloride by mouth; one, a child of nine, was maintained for four months and then died; the other, a man of twenty-two, is still alive and well four and one-half months after the commencement of the treatment. In both the size of the heart was markedly increased after the first administration. This paralleled an increase in blood volume and in blood urea and a fall in hæmoglobin concentration. The heart returned to its previous size when the sodium chloride was discontinued. Sodium and calcium balances were done. The child was more difficult to keep in positive sodium balance than the adult and went into increasing negative balance before death. The symptoms preceding death were typical of hypoglycæmia and the blood sugar was 0.020 g. per cent four hours before death. This patient did not present the dehydration syndrome of the usual Addison's death blood volume, blood urea and blood sodium being normal. In the adult, treatment with sodium chloride reduced the blood urea level to very low levels (3.7 mg. of urea-nitrogen per cent). On giving 15 g. of urea at this stage it was excreted slowly over a period of 72 hours and 4 g. were retained. The blood urea-nitrogen was 11 mg. at the end of this period. A further 15 g. of urea were then given and the whole amount excreted in eighteen hours. The excretion of chloride and of creatine and creatinine in the urine was also studied, and nitrogen and potassium balances are being done.

**SOME OBSERVATIONS ON THE TEMPERATURE OF  
THE RIGHT AND LEFT HEART BLOOD**, by Ronald  
V. Christie.

The temperatures were measured by copper-constantan thermocouples, the leads being enclosed in fine ureteral catheters. These can easily be introduced into the larger arteries or veins of the dog or cat, and, if suitably lubricated, can be inserted for any distance without the formation of blood clots. One couple is inserted into the femoral vein until the tip lies at the opening of the inferior vena cava into the right auricle. The arterial couple is inserted into the femoral or carotid artery. The couples are balanced directly one against the other, and with a high voltage sensitivity galvanometer, critically damped, the temperature difference between the two thermocouples can be easily

read to  $1/400^{\circ}$  C. with single copper-constantan junctions.

It was found that the temperature of the right heart blood was as an average  $0.12^{\circ}$  C. higher than that of the left heart blood, and that only between 10 and 20 per cent of the heat loss which this represents was due to the evaporation of moisture in the lungs, the rest being due to the excretion of  $\text{CO}_2$ .

The significance of this method with regard to the measurement of the heat of combination of  $\text{CO}_2$  and  $\text{O}_2$  in the blood, the cardiac output, and the circulation velocity through the lungs was discussed.

**THE BEHAVIOUR OF THE SERUM IRON IN CERTAIN  
TYPES OF ANÆMIA**, by John F. McIntosh.

Following the work of Bunge, and of Hausermann and Abderhalden, it was generally supposed that there was no free or loosely combined iron in the blood plasma. With improvement in analytical methods it has become clear that such iron is present in measurable quantity, but there is still some uncertainty as to its amount, and practically no information as to its physiological significance.

A clinical study of the serum iron has been carried out. Serum from defibrinated blood was precipitated in 5 per cent trichloroacetic acid. The organic matter was oxidized with sulphuric acid and potassium chlorate, and the iron determined colorimetrically as the thiocyanate. By this method, the iron content of normal human serum has been found to be of the order of 0.1 mg. per cent. This value is in substantial agreement with the findings of Fontès and Thivolle, and of Barkan, Warburg, Guthmann, Locke, and their respective co-workers. Considerably higher values have been reported by Riecker, and by Marlow and Taylor.

Curves obtained by repeated determinations of the serum iron give the clearest picture of its behaviour. Low values have been found during the anæmia which follows hæmorrhage. This is best known in the experimental animal. In a dog, the serum iron fell from 0.17 to 0.08 mg. per cent after bleeding, and remained low throughout the period of hæmoglobin regeneration. After the hæmoglobin value had reached normal, the serum iron returned to its initial value. From this experiment we learn that blood formation has a powerful influence in depressing the serum iron. This fact must be kept in mind when we compare the following clinical cases. In the disease known as hypochromic microcytic anæmia it is possible to cure the patient by administration of iron. It is therefore supposed that the anæmia is due to a lack of available iron in the body. We might reasonably expect that in an untreated case the serum iron would be low. This is found to be true. During iron medication, the hæmoglobin



tends to rise first, the serum iron, later. The curves show that narrow fluctuations in the hæmoglobin are accompanied by wide changes in the serum iron. From these cases we learn that iron given by mouth is taken up rapidly by the hæmatopoietic organs, and possibly by the iron depots, so that the iron in the serum remains low so long as there is any need for it. Here the low serum iron indicates a lack of iron. In pernicious anæmia it is well known that iron therapy is of no value. We should not expect to find low serum iron values during relapse. In an untreated case a high initial value of 0.24 mg. per cent was found. During the reticulocytosis produced by liver extract, the value fell to 0.04 mg., then rose gradually as treatment was carried on. It is well known that in pernicious anæmia the iron depots are stored with sufficient iron to make up the deficit in hæmoglobin. Hence we see that the low serum iron values in this case do not indicate a lack of iron on the part of the body.

One might ask whether these findings have a practical significance aside from their physiological and theoretical interest. The following generalizations might be made in a tentative way. In any case of anæmia in which the serum iron is high we may expect no benefit from iron therapy; if the serum iron is low, it may indicate a deficiency in iron, but we cannot be sure of this without the consideration of other data.

**A PHOTOELECTRIC METHOD FOR THE MEASUREMENT OF THE NUMBER OF RED CELLS AND HÆMOGLOBIN CONCENTRATION IN THE SAME SMALL SAMPLE OF BLOOD**, by Kenneth A. Evelyn and Ronald V. Christie.

The apparatus is essentially a photoelectric opacity meter, consisting of a light source, adjustable filter, absorption cell, photoelectric cell and galvanometer. The light source is a 2 c.p. 6 volt bulb in a parabolic reflector. The conventional rectangular glass absorption cell is replaced by a test tube which also serves as a cylindrical lens to focus the light on the photocell. A vacuum alkali cell is used for maximum stability. A filter which transmits only the red end of the spectrum (in which region absorption by hæmoglobin is negligible) is inserted; 0.05 c.c. of blood is diluted to 10 c.c. in the absorption tube, and is further diluted until the opacity falls to a value which corresponds to a known concentration of erythrocytes of normal size. The erythrocyte concentration is calculated from the dilution required. The cell diameter is measured on a halometer attached to the apparatus and a correction applied if necessary (the correction for size is negligible except in extreme cases).

The sample is laked with saponin, the filter changed to transmit a band including both main

hæmoglobin bands, and the hæmoglobin concentration measured as on any other photoelectric hæmoglobinometer.

Errors in the erythrocyte count are  $\pm 5$  per cent; in the hæmoglobin concentration,  $\pm 2$  per cent. The technique is simple, the apparatus inexpensive, and the entire determination requires four minutes.

### The Ontario Neuro-Psychiatric Association

The annual meeting of the Ontario Neuro-Psychiatric Association for the year 1934 was held at the Homewood Sanitarium, Guelph, on May 18, 1934. The President, Dr. W. C. Herriman, was in the Chair. Dr. Harvey Clare, Superintendent of the Homewood Sanitarium, gave the address of welcome. Papers were read by Burdett H. McNeel, B.A., of the Ontario Hospital, Whitby, Dr. W. H. Lowry, of Toronto, and Dr. N. B. Taylor, Professor of Physiology in the University of Toronto. Dr. E. P. Lewis, of the Toronto Psychiatric Hospital, was the guest speaker at the Association dinner. The following officers were elected for the coming year:

*Honorary President*, The Honorable Dr. J. M. Robb; *President*, Dr. T. D. Cumberland; *Vice-president*, Dr. George Kidd; *Secretary*, Dr. A. McCausland. *Executive Committee*: Drs. B. T. McGhie, R. G. Armour, H. A. McKay, G. H. Stevenson, D. O'G. Lynch, and J. McGeoch. *Editorial Board*: Drs. B. T. McGhie, C. B. Farrar, D. R. Fletcher, J. P. S. Cathcart, J. A. Hannah.

A. McCAUSLAND,  
*Secretary.*

### The Winnipeg Medical Society

The annual meeting of the Winnipeg Medical Society was held on May 25th. The retiring president, Dr. A. P. MacKinnon, delivered the presidential address on "Gardening as a medical hobby". The election of officers resulted as follows:

*President*, Dr. W. W. Musgrove; *Vice-president*, Dr. L. D. Collin, St. Boniface; *Secretary*, Dr. O. C. Trainor; *Treasurer*, Dr. C. E. Corrigan; *Trustee*, Dr. A. W. Hogg.

ROSS MITCHELL

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Any one who wishes to become a good writer should endeavour, before he allows himself to be tempted by the more showy qualities, to be direct, simple, brief, vigorous, and lucid.—The King's English.



## University Notes

### University of Manitoba Medical College

The clinical week, held from May 14th to 19th, to commemorate the fiftieth anniversary of the founding of the Medical College was a decided success in attendance, interest and quality of the program. Over one hundred and seventy were registered for the full course, and this number included doctors from Alberta, Saskatchewan, Ontario, North Dakota and rural Manitoba as well as from Winnipeg. The open meetings, such as those on the evening of the 15th, addressed by Dr. N. M. Keith, Rochester, Minn., and Dr. A. A. Fletcher, Toronto, and the Gordon Bell Memorial Lecture on the 18th, given by Prof. William Boyd, were crowded to capacity.

Those responsible for the Clinical Week are much indebted to the visiting speakers who made such a valuable contribution to the programs:— Dr. Owen H. Wangenstein, Professor of Surgery, University of Manitoba; Dr. J. G. FitzGerald, Dean of the Faculty of Medicine, University of Toronto; Dr. Egerton Pope, Professor of Medicine, University of Alberta; Dr. R. L. McGibbon, Professor of Anatomy, University of Saskatoon; Dr. N. M. Keith, Rochester, Minn., and Dr. A. A. Fletcher, Toronto.

The ceremonial meeting on the opening night was colourful with academic dress. Dean A. T. Mathers presided and Dean FitzGerald, of Toronto, on behalf of his own and other Canadian universities, tendered their congratulations to Manitoba. The venerable Chancellor of the University, Archbishop Matheson, and Premier John Bracken also extended congratulations on behalf of the University and the Province of Manitoba. Dr. D. A. Stewart gave a brilliant address on "Medicine in fifty years", after which a reception was held in the Assembly Room of the Winnipeg Auditorium.

In the Gordon Bell Memorial Lecture Professor Boyd spoke on "Growth—normal and abnormal", pointing out how aberrant growth led to malignancy, but emphasizing the fact that many forms of cancer were curable and had been cured. In introducing him, Dr. A. P. MacKinnon, President of the Winnipeg Medical Society, paid tribute to the sterling qualities of the late Dr. Gordon Bell.

The program was designed to be as practical and helpful as possible. Special interest centred in the small group clinics and demonstrations covering a wide range of subjects.

The social side of the meeting was upheld in four luncheons, a dinner and dance, and a tea given by Mrs. Gordon Fahrni in honour of the wives of the visiting doctors. The luncheons were addressed by Dean J. G. FitzGerald, on

"The place of preventive medicine in the medical curriculum"; Prof. R. L. McGibbon, on "Flights from medicine"; Prof. E. L. Pope, on "Plain tales from the foothills", and Dr. S. C. Peterson on "Neisserian infection". At the alumni dinner, presided over by Dr. W. W. Musgrove, Dr. Bruce Chown proposed the toast "Our Teachers", which was responded to by Dr. H. H. Chown, the beloved dean from 1900 to 1917. Views of the thirteen incorporators and the various buildings which have housed the college were shown. Dean Mathers, replying to the toast of "The College", pointed out its present position, and spoke of plans for the future.

The spirit of the whole week was caught in a cartoon by Arch Dale in the *Winnipeg Free Press* in which "Old Doc Manitoba," applying a stethoscope to the chest of a stalwart and smiling young man, labelled "Medical College", exclaims: "Fifty Years Old this week—and sound as a bell."

### McGill University

The Annual Convocation of McGill University was held on May 29, 1934, when 505 degrees in the various faculties were conferred.

The Honorary Degree of Doctor of Laws was conferred on Edgar Douglas Adrian, Foulerton Professor of the Royal Society, and Fellow of Trinity College, Cambridge, winner, with Sir Charles Sherrington, of the Nobel Prize in 1932; Frederick M. Becket, President of the American Institute of Mining Engineers; Seraphin Boucher, Director of the Department of Health, Montreal; Robert H. Coats, Director of the Dominion Bureau of Statistics; and the Hon. Hugh Edwin Munroe, Lieutenant-Governor of Saskatchewan.

The degree of Doctor of Medicine and Master of Surgery was conferred on seventy-nine candidates. The prize winners were the following.

William R. Foote, B.A., Vancouver, B.C., the Holmes Gold Medal for the Highest Aggregate in all subjects of the medical curriculum; the Alexander D. Stewart Prize for the Highest General Qualifications for the Practice of Medicine.

W. H. Philip Hill, B.A., Montreal, the J. Francis Williams Fellowship in Medicine and Clinical Medicine (equal).

Arthur C. Corcoran, B.A., Waterloo, Que., the J. Francis Williams Fellowship in Medicine and Clinical Medicine (equal).

John V. Nicholls, B.A., Montreal, the Wood Gold Medal for the best Clinical Examinations in the Final Year.

Curtis R. Lacy, B.Sc., Freehold, N.Y., the Lieutenant-Governor's Silver Medal for the Highest Standing in Public Health and Preventive Medicine.

### The University of Toronto

Medals, prizes, scholarships and Fellowships awarded by the Senate of the University, Faculty of Medicine.

*Sixth year.*—Gold Medal, Miss J. C. Gray, B.A.; Silver Medal, T. Kajiyama, B.A.; Silver Medal, R. C. Dickson; The Ellen Mickle Fellowship, R. L. Noble; The Chappell Prize in Clinical Medicine, Miss J. C. Gray, B.A.; The Ontario Medical Association Prize in Preventive Medicine, Miss J. C. Gray, B.A.; The David Dunlap Scholarship, R. L. Noble; The Canadian Medical Institute Prize, R. C. Dickson.

*Undergraduate.*—The David Dunlap Scholarships: fifth year, no recommendation; third year, J. L. Cathie; The Baptie Scholarship, T. P. Keast, B.Comm.

*Graduate.*—The Reeve Prize, D. L. Selby, B.A., M.D.; The Lister Prize in Surgery, H. F. Mowat, M.D.

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## Special Correspondence

### The Edinburgh Letter

(From our own Correspondent)

Lord Macmillan made some interesting comments regarding the expert witness in the course of a lecture recently delivered before the Royal Medico-Psychological Association. There was in these days, he said, an increasing resort to the particular type of professional man known as the expert. The maladies of the world had become so acute that the specialist has had to be called in for consultation. The results were not always too happy. The expert mind tended to have failings as well as excellences. The attaining of highly specialized knowledge in one subject was apt to create the arrogance of assurance. There was also the tendency of experts to differ. On the other hand, the value of the specialized knowledge was incontestable. In Court irritation under cross-examination might well lead the expert to make confident assertions which he might have occasion later to regret. Fair cross-examination was one of the best means of eliciting and testing the truth, but not all cross-examination was fair. It was in some form of consultative capacity that the abilities of professional men were best utilized in the public service. Lord Macmillan then proceeded to discuss the various types of professional mind. There was probably no professional type which throughout the ages had been more subject to depreciatory comment than the legal mind. The conception of the advocate as a kind of artful dodger, who made his living by stupifying his conscience, was, however, utterly

remote from the truth. The lawyer, it had to be admitted, tended to foster certain intellectual habits, which, if they became exaggerated, were not admirable. Preoccupation with words had its dangers. The legal mind was unduly critical, and often handicapped the lawyer in dealing with constructive proposals. Thus lawyers were not temperamentally well fitted for leadership, either in politics or business, in both of which spheres the adventurous spirit was needed. On the medical mind he made the following observations. The effect of constant contact with human suffering could not but be profound. The doctor had to acquire a certain calmness in the presence of emergency and tragedy, and this was apt to be mistaken for unconcern. The doctor might tend to become oracular, but unselfishness and devotion to duty far outweighed any of the foibles which might lead to this charge. It was perhaps in the medical man that the professional mind found its finest sphere. The clerical mind was perhaps the most distinctive type of all. It was the essence of the clergyman's vocation that he should be unworldly. There were, however, the intellectual dangers of dogmatism, with its ugly companions, intolerance, persecution, and casuistry, with its accompanying lack of candour. Clericalism and sacerdotalism were not attractive things. On the other hand, there were long records of many saintly lives.

The College for unemployed men and women which has been established in Edinburgh through the generosity of Prof. D. P. D. Wilkie, and which was opened last October by Sir James Barrie is doing a splendid work. It has become known as "The Working Man's University". The three main activities of the College are occupational training (chiefly carpentry, but also cobbling, weaving and metal work), physical training, and evening classes. The subjects chosen by the men for their evening classes are rather interesting. They include economics and the economic history of Scotland, languages, geography, drama, and the study of wireless. The class in the latter subject is the largest, but after that comes the class in German, there being about 100 men learning German. The eagerness of the men to learn German is due to the fact that some of them had picked up a little knowledge of the language while they were in the Army of Occupation, and the desire to learn more seems to be caused by the Hitler movement. It is not that the men are of Nazi sympathy, but the movement has aroused their keen interest. The discussion groups have been of great value in teaching logical and reasoned argument. None of the discussions, which are superintended by a university lecturer or student, are allowed to become irrelevant or illogical in character. The women are chiefly learning cooking, physiology,



and the study of health. They are also being given physical training. There can be no doubt that the College has already proved of great value to those who attend it. It is inspiring to see the men at work and to see the change on their outlook on life. They are being made physically fit and given a real start in adult education. In this way the industrial depression, which has caused the establishment of such centres all over the country, has been a blessing in disguise.

A proposal that doctors' motor cars should be exempt from the speed limit restrictions as is permitted to ambulances, fire-engines, and police cars was recently discussed by the House of Commons' Committee which is considering the new Road Traffic Bill. An amendment was considered, the purpose of which was to give vehicles "used for medical purposes" exemption from the speed limit which the Bill proposes to impose in "built up areas". The Minister of Transport in speaking against the amendment said that the amendment would make any doctor free from the speed limit on any occasion. Every attempt to exempt a car which could not be clearly distinguished was liable to lead to the very delay they were anxious to avoid. He agreed that there was some substance in the proposal, but confessed himself unable to see any way out of the difficulty. No Court would convict if a doctor had exceeded the speed limit in a real emergency, nor, in fact, would the police ever issue a summons in such a case.

R. W. CRAIG.

7 Drumsheugh Gardens,  
Edinburgh.

### The London Letter

(From our own Correspondent)

By far the most important event of the past few weeks has been the demonstration of "cineradiography" before the Royal Society of Medicine. Dr. Russell Reynolds, of London, and Dr. Robert Jankin, of Bonn, the pioneers who have been working independently on the subject, were both present to expound their views and demonstrate their films. Indirect methods seem to offer the most scope, and at present, common to both workers, is a system whereby shadows on a fluorescent screen are photographed by an ordinary film camera. The total length of exposure imposes some limitations at present for work with human subjects, but Dr. Jankin was able to show such spectacular pictures of animals that it is obviously merely a question of technique before equally good illustrations of the movement of human organs are available. Dr. Reynolds has devised a neat way of surmounting the difficulty about length of exposure by taking a short film and

then joining many copies of this end to end so that the total length represents a repetition of the same movements (say, of the stomach) which can be studied in detail from the film. The possible applications of cineradiography for the teaching of anatomy and physiology are immense. When sound is also harnessed to the film there will be great scope for research and the stethoscope may well be the object of criticism as a result. Those present at the meeting early in May had the impression that they were certainly assisting at an epoch-making event.

Another event which may also mark an epoch has taken place this month in the establishment of a Clinical Research Unit at Middlesex Hospital. The unusual feature of the proposal is that the unit is to be under the control of the scientific and research side of the medical school staff. The professors of biochemistry, pathology and physiology will have direct contact with and share the responsibility in the treatment and care of patients admitted to the unit. The stay of such patients will be dictated by the necessity of investigation rather than by the usual considerations such as pressure of a long waiting list. In all, the unit is to consist of about 15 beds, in small wards of one to three beds, and besides offices and small test-rooms there is to be a clinical lecture theatre. The revolutionary feature of the proposal, for this country, is the delegation by the managing board of responsibility to the purely scientific rather than the clinical staff of the hospital. For the development of medical science this represents a very important step.

After all the controversy on diet and the differences between the British Medical Association's Committee and the Ministry of Health's Committee, a typically British compromise has been reached. The British Medical Association's committee was concerned with single active families and the Ministry's committee with communities of people, many of whom lead inactive lives. Hence is explained the divergencies as regards total calories and the provision of first-class protein. The joint conference, in their report "deplore the exaggerated importance attached to the alleged disagreement", but the outside observers cannot help the impression that the British Medical Association have won the struggle! This is especially true as regards the views of the conference on first-class animal protein and the value of milk for children. It is good that the subject has been so thoroughly ventilated, and there is no excuse now for ignorance on the fundamental facts of diet.

An indication of the modern trend of preventive medicine is to be found in the recent meeting of the Royal Institute of Public Health at Norwich when one sectional meeting discussed the organized treatment of motor



accidents. A scheme for the early treatment of road injuries was discussed, with striking analogies with the organization of war-time for dealing with the wounded. The futility in rural districts of taking an accident case direct to the surgery of the local general practitioner was indicated, as he would probably be out on his rounds. Obviously the problem is complex, and involves not only the immediate treatment but the whole question of the repair of structure and restoration of function. Now that the question of payment for road accident cases in hospital has been more satisfactorily settled the next step would seem to be some better scheme for their general care and treatment.

ALAN MONCRIEFF.

121 Harley St.,  
London, W.1.

## Letters, Notes and Queries

### The British Industries House

*To the Editor:*

As Chairman of the Medical Advisory Council of the Medical Section of British Industries House, I hope you will allow me to bring to the notice of your readers an enterprise which, we believe, will be of considerable interest to them.

When I was Medical Secretary of the British Medical Association, I was frequently visited by doctors from overseas who had been commissioned to buy furniture or apparatus for their hospitals, and who wished to know if there was any place at which they could see things under one roof. There was no such place, but at British Industries House there soon will be.

This Institution, which is backed by a combination of six of the largest insurance companies in this country, is situated in a very large building at Marble Arch, Oxford Street, London, W.1., which was built for Messrs. Gamage, and, not being successful in their hands, was bought by the insurance companies. It covers a very large floor space, and it is intended to offer to manufacturers and buyers a centre at which goods of exclusively British manufacture can be seen. One floor will be reserved for medical instruments, drugs, and other goods suitable for medical men and medical institutions. The building will not be open to the public, as it is intended to be a real business centre. It has the cordial support of many leaders of commerce in this country, together with the Department of Overseas

Trade, and is already assured of the active participation of many of the chief manufacturers of British drugs, instruments and hospital requirements.

In establishing the Medical Section, the Directors appointed a small Medical Advisory Council, consisting of Sir Crisp English, F.R.C.S., of St. George's Hospital, Dr. E. P. Poulton, of Guy's Hospital, and Mr. A. R. Melhuish, a Past-president of the Pharmaceutical Society of Great Britain, with myself, to guide them in making the section useful and attractive to the medical and pharmaceutical profession.

Doctors, pharmacists, and hospital managers, as potential buyers, will be admitted, on presentation of their card. The section will be opened on July 18th, just before the opening of the Annual Meeting of the British Medical Association at Bournemouth, and further particulars will be announced later. Any of your readers who may be in this country will be welcomed at all times to the section. I feel sure that the project will be a useful one, and will be warmly welcomed by all who have ever had to spend their time in journeying to various places in order to examine goods of British manufacture in which they are interested.

ALFRED COX,

*Chairman, Medical Advisory Council.*

London, W.1,  
April 11, 1934.

## Topics of Current Interest

### The Efficiency of Masks

The gauze mask is so established a feature of operative surgical and obstetric work that its capacity to do what is expected of it may be taken too much for granted. Indeed, according to some investigators, it appears to be almost useless. The masks used in sixty American hospitals were procured by Walker,<sup>1</sup> and were of twenty-two different types: of these, fifteen were discarded because they "could not possibly be germ-proof"; the remaining seven were tested on a streptococcus carrier, who read aloud for fifteen minutes with an exposed culture plate eighteen inches from his mouth, and streptococci were grown in varying numbers in tests with every one. Walker recommends a mask consisting of sheet rubber between layers of gauze; and, although it might be expected that bacteria would be expelled in the current of air at the sides of this contrivance, they apparently were not. A similar conclusion is reached from a more recent study by Blatt and Dale,<sup>2</sup> who tested masks composed of various

Answers to questions appearing in this column should be sent to the Editor, 3640 University Street, Montreal.

1. *Surg., Gyn. & Obst.*, 1930, 50: 266.

2. *Ibid.*, 1933, 57: 363.

materials, some of which were treated with antiseptics, on subjects who coughed into an enclosed space in which culture plates were exposed at different distances. No permeable mask of any material, however treated, was found effective, and the number of bacteria escaping was considerably greater if the mask had previously been worn for some time. Satisfactory results were only obtained with a mask consisting of cellophane enclosed between layers of gauze, and the air discharged at the side of this was said to be "practically sterile": it was assumed that when the current of air from the mouth is deflected by the mask, particles of moisture "continue forward by virtue of their momentum," strike the mask, and adhere to it. There appears to be only one claim that any permeable mask is effective: this is made by Cann<sup>1</sup> for the obstetric mask used at Guy's Hospital, which consists of no fewer than sixteen layers of gauze. The methods used in these tests are by no means uniform, and in some cases not beyond criticism, but where they appear to err it is in the direction of insufficient stringency. It may safely be concluded that a thin gauze mask does no more than arrest the gross splash of a cough or sneeze; against "droplet infection" in the sense of the more numerous small particles expelled during ordinary speech, it is not a barrier. If the conclusions of Walker and of Blatt and Dale be accepted, an impermeable mask is capable of arresting these by deflection from an absorbent surface. Such investigations as these prompt the reflection that there is still much to be learned about droplet infection, and particularly about the droplet itself, its size, its speed of fall in still air, its length of survival as a fluid under different air conditions of temperature and moisture, and the properties of the particle which must remain after evaporation. This mechanism is concerned in transmitting so many infections that useful preventive lessons might well be learned from its study.—*Brit. M. J.*, 1933, 2: 1039.

### Osteopathy

(A Letter to "The Times")

The letter in your issue of the 16th inst. from Major-General Lord Edward Gleichen, in which he once more appears as mentor of the medical profession, raises questions of greater public importance than osteopathy. Why is it that all and sundry "rush in" and give opinions on difficult medical problems when they are unacquainted with such sciences as anatomy, physiology, and pathology which condition their understanding?

Supposing I were to talk in the same glib way about engineering, to lecture the Judges on, say, the Law of Property, or tell soldiers how to arrange the defences of London against

air attack, would it not be promptly intimated to me that I should either shut up or be shut up? Why then is medicine, despite its complexities, singled out for different treatment? The answer is that the public think of medicine in terms of magic, and not in terms of science.

Time ago doctors did the same. During the past 100 years medicine has espoused and faithfully pursued the scientific method. Has the harvest of knowledge thus garnered been surpassed in any other walk of life? To mention a few examples. Pasteur and Lister gave us aseptic surgery; Koch, Wright, and Leishman bacteriology and the conquest of typhoid; Manson, Bruce, Ross, and Gorgas showed the way of deliverance from malaria, sleeping sickness, and other tropical diseases. In more recent days Mackenzie and Lewis have given us new knowledge on heart disease; Robert Jones on diseases of bones and joints; Hopkins and the Mellanbys on vitamins; Minot on the anæmias; the wonderful rôle of hormones is now unfolding with implications the extent of which we can hardly yet envisage.

Respect for your space restrains my theme, but has not enough been said to demonstrate that the science of medicine is on the right path? The extension of this path step by step into the unknown will be difficult always, mistaken sometimes, but increasingly fruitful. "Narrow is the way which leadeth unto life."

Does it not follow that if the public is to profit by new knowledge the first desideratum is sound training of students? We are the best judges of what that training should be. In undergraduate life education is concerned with the basic sciences, the general study of disease in the living and the dead, and the vital subject of diagnosis. Competency after this training, tested by examination and testified by medical qualification, is essential for the status of a doctor.

If the osteopath wishes to escape that test he has open to him the honourable status which belongs to, say, the masseur and radiographer. Both the masseur and the osteopath have the gift of "hands," though the work of the former has a sounder scientific basis than the latter. We welcome the contributions of both to the art of healing. It needs diagnosis by a qualified doctor to say whether a given case is suitable or not for their treatment, as has been pointed out by Sir Robert McCarrison. The disasters which sometimes follow osteopathy are due not to faulty craftsmanship but its application to the wrong cases.

If, on the other hand, the osteopath desires the status of a doctor he must pass that test. There can be no back entrance.

Major-General Lord Edward Gleichen, with his freedom of criticism of a profession not his own, says we are stubborn. It is right to be stubborn where truth is concerned. A man



presents himself for the post of chief engineer to an Atlantic liner. He is asked for evidence of the prescribed training as testified by the Board of Trade certificates. Says the candidate, "I have a special training of my own; I am so gifted as not to require the training and tests you prescribe." We know what the answer of the Board of Trade would be. Our answer is similar.

DAWSON OF PENN.

—*The Times*, Nov. 18, 1933.

### Are More Doctors Needed?

The evils of overproduction in many fields have been vehemently discussed of late. The spotlight has been turned on surpluses of cotton and corn, but little has been said of the graver menace of excess production of physicians. The Commission on Medical Education in its final report a year ago pointed out that the ratio of doctors to population was increasing. Elsewhere in this issue of the *Journal*, the Council on Medical Education and Hospitals presents its annual compilation of the reports of the state board of medical examiners. In 1933, 5,012 persons were added to the medical profession through licensure, the losses by death for the same period being approximately 3,500. The net gain, 1,500, is about 1 per cent of the number of physicians actually practising in the United States. The census of 1930 shows an increase in population during the preceding decade of 6 per cent, or an annual rate of increase that is something less than six-tenths of 1 per cent. Since all students of the question agree that the rate of increase is diminishing and that the country is tending toward a stable population, it is evident that the medical profession is increasing faster than the general population, and that unless the states promptly initiate measures to restrict the number of those licensed to practise medicine a great surplus of unemployed doctors will become apparent. The social implications of such a condition would by comparison render the well known surfeit of agricultural products relatively innocuous.—*J. Am. M. Ass.*, 1934, 102: 1402.

That in literature, as in society, good form is useful we are now to learn, but in the amenities of form it shall not be said of us that in a coxcombry of manners we become too exquisite for the primary forces of the human mind.—Notes on the Composition of Scientific Papers.

## Abstracts from Current Literature

### Medicine

**Achlorhydria.** Oliver, T. H. and Wilkinson, J. F., *Quart. J. of Med.*, 1933, 2: 431.

The authors present a critical review of the whole subject of achlorhydria. Achlorhydria denotes "the absolute deficiency of hydrochloric acid," while achylia gastrica strictly means "the complete absence of all gastric secretions", although even in the most severe cases, some mucus and a varying amount of watery fluid containing some chloride are secreted. Achlorhydria would appear to be twice as common in women as in men. It is not often found in healthy individuals, and is often the forerunner of disease developing many years later. Of recent years, with the introduction of gastric stimulants, such as histamine, it has been found that, while achlorhydria is comparatively common, achylia is rare, except in cases of pernicious anæmia. There seems to be a marked family tendency to achlorhydria, and a family history of anæmia, allergic disease or rheumatoid arthritis is frequent.

The incidence increases markedly in later life. Etiologically, the condition may be (1) familial—due to a constitutional abnormality, (2) due to chronic gastritis, caused by direct irritation or by hæmatogenous toxins, or (3) of neurogenic origin. There is evidence favouring all three theories.

Certain functional disturbances — neurasthenia, flatulence, irregularity of the bowels, debility, slight anæmia, sore tongue—are commonly associated and a combination of several of these symptoms may produce a picture hitherto often diagnosed as a neurotic dyspepsia. The authors believe this picture should be regarded as a true achlorhydric syndrome, which is often present along with rheumatoid arthritis or with some allergic manifestation. Achlorhydria is often present in organic gastrointestinal diseases such as chronic gastritis, gastric or intestinal cancer, colitis or dysentery. It has been regarded as evidence of chronic gastritis, which in turn has been held to be a precursor of cancer of the stomach; the sex incidence and the infrequency of association of the achlorhydric anæmias with cancer, however, would suggest that it is not an important factor.

Gastric ulcers quite commonly, but duodenal ulcers rarely show achlorhydria. Some achlorhydrics have intense pain, suggestive of ulcer, and radiologically show gastric hypermotility and intense pylorospasm, which may account for this pain. Achlorhydria is common in cholecystitis and liver diseases. It is almost constant in pernicious anæmia and subacute



combined degeneration of the cord. It is also frequently associated with microcytic anæmias and is an important factor in their development. It is common in thyroid disease, diabetes and rheumatoid arthritis. Individuals suffering from allergic diseases, as asthma, migraine and urticaria, and also from such dermatoses as rosacea and psoriasis, will frequently exhibit it. When achlorhydria appears to be giving rise to symptoms it should be treated. Attempts may be made to induce the impaired gastric mucosa to secrete again—as by repeated lavage with hydrogen peroxide as advocated by Hurst. This method is useless in achylia gastrica, of course. The other method is to remedy the deficiency by adequate doses of hydrochloric acid and pepsin—such a dose being 30 minims of dilute hydrochloric acid (B.P.) with glycerine of pepsin, 3 i or ii. In the functional cases with dyspepsia and diarrhoea, very satisfactory results are the rule; in patients with organic disease, the general health is often improved. Hydrochloric acid is invaluable in pernicious anæmia for relieving any dyspeptic symptoms which may be present; it does not seem to be necessary when hog's stomach therapy is used.

W. FORD CONNELL

#### Syndrome of Anæmia, Glossitis and Dysphagia.

Suzman, M. M., *Arch. Int. Med.*, 1933, 51: 1.

The syndrome of anæmia, glossitis and dysphagia, often referred to as the "Plummer-Vinson syndrome", was first pointed out independently by Kelly and Paterson at the Royal Society of Medicine in London in 1919. Since then numerous cases have been reported in the literature. Various theories have been advanced to explain the condition, which occurs chiefly in middle-aged women.

The author presents the reports of 8 cases studied at the Massachusetts General Hospital, together with the autopsy findings in one case. The incidence was restricted to women, and the age varied from 27 to 61 years of age. Anæmia of the hypochromic type was a constant finding, with an average hæmoglobin of 50 per cent. Difficulty in swallowing was usually referred to the level of the thyroid. Atrophy of the mucous membrane of the tongue, cracks and fissures at the corners of the mouth were noted. Loss of weight, dyspnoea, weakness, and paræsthesias were inconstant. One case showed well marked spoon-shaped deformity, with longitudinal splitting of the finger nails. Free hydrochloric acid was present only once in the five gastric analyses.

The treatment consisted of iron in large doses (iron and ammonium citrate, 90 grs. daily), a high caloric diet, and dilatation of œsophageal strictures. A marked improvement occurred in all cases except one, where the

filiform bougie perforated the œsophageal wall producing mediastinitis and death.

In discussing the etiology of this condition the author refutes the older theories of spasm, achalasia, and syphilis and suggests that it be considered as a syndrome that may arise as a complication or concomitant manifestation of idiopathic hypochromic anæmia. He points out that, except for the dysphagia, all the manifestations of this syndrome, including the response to iron therapy, are indistinguishable from those of the latter. He further states, that, since the administration of iron almost invariably relieves the anæmia and usually alleviates the lesions of the tongue and mouth, a virtual deficiency of this metal may play some part in the etiology of this disease, be it a lack of supply, a failure of absorption, or an inability to utilize the metal.

L. J. ADAMS

#### Coexistence of Pernicious Anæmia and Lesions of the Gastrointestinal Tract. I. Carcinoma of the Stomach. Conner, H. M. and Birkland, I. W., *Ann. Int. Med.*, 1933, 7: 89.

The authors report 11 cases in which the coexistence of pernicious anæmia and carcinoma of the stomach was practically certain. In 7, the diagnosis of carcinoma was proved at operation; in 1, at autopsy. In 3, the diagnosis of inoperable carcinoma of the stomach was made by the roentgenologist. The diagnosis of pernicious anæmia was carefully made in each case. In 6 cases, the sequence of the two diseases as to incidence could not be established. In 3, the carcinoma seemed to follow the pernicious anæmia (by seven years, one and a half years, and seven to eight years). In one case, pernicious anæmia was diagnosed 32 months after partial resection of the stomach for carcinoma. In another case, pernicious anæmia was diagnosed six years after a similar operation.

A search for carcinoma should be made in cases of pernicious anæmia, especially when the patient has lost much weight. When both diseases are present, specific treatment should be instituted before operation for the carcinoma, in order to avoid serious consequences from the anæmia, and to forestall, if possible, neurological complications.

H. GODFREY BIRD

#### A Clinical Conception of Rheumatic Heart Disease. Levine, S. A., *Am. Heart J.*, 1933, 9: 26.

The author herein presents a side of the problem of rheumatic heart disease that has received little attention, namely, the condition of the host or patient, the internal environment in which the disease develops, and, especially, the possible rôle the glands of internal secretion may be playing. As is pointed out, the responses of the human body to outside influences, whether

they be physical, chemical, bacterial, or psychic, are not only most variable but also difficult to predict. Not only do human beings differ from each other but each one differs from year to year or month to month in his bodily behaviour, physical, anatomical and chemical make-up, and, presumably, in the biological reactions to bacteriological invasions. If, as has been assumed, the streptococci play such an important part in the disease, and, as we know, there is a failure to develop lasting immunity to recurrence, why is it that such a small part of the population develop the disease? It must be, therefore, assumed that it is the condition of the host that determines whether the disease develops and what form it takes. Why does one develop chorea, another polyarticular rheumatism, a third skin lesions, a fourth pericarditis, and a fifth fever and anaemia without gross cardiac or arthritic involvement? "Growing pains", which are assumed to be rheumatic, disappear when the proper endocrine balance, possibly pituitary, has been established. The author suggests that herein is a basis for research and that a study of the influence of the glands of internal secretion on this disease would prove fruitful.

W. H. HATFIELD

**Thrombo-Phlebitis in Acute Rheumatism.** Perry, C. B., *The Lancet*, 1933, 225: 966.

After a brief but complete historical summary beginning with the recognition of the possibility of a rheumatic phlebitis by Bouillaud in 1840, the authors describe three cases of venous thrombosis occurring during the course of acute articular rheumatism in childhood. Clinically, there is pain over the vein involved, developing during the course of an acute rheumatic fever with cardiac involvement, followed later by oedema and swelling of the area drained by the vein. The occurrence of pain one or two days before swelling suggests a primary phlebitis antecedent to the secondary thrombosis. The post-mortem findings in these cases show thrombi in the veins with hyperaemia and small round-cell infiltration of the adventitia and surrounding tissue, and in one case definite endothelial cell proliferation in the vein wall resembling the Aschoff nodules found in the heart. From these results it is concluded that a rheumatic phlebitis may occur as a rare feature of acute rheumatism.

GUY H. FISK

**Primary Carcinoma of the Lung.** Hruby, A. J. and Sweany, H. C., *Arch. Int. Med.*, 1933, 52: 497.

That the number of cases of cancer of the lung coming to autopsy within the last forty years has increased tenfold is a well established fact. On the other hand, opinions vary greatly

as to whether an actual increase in the general incidence exists. The authors offer a partial explanation of the apparent increase on the basis of the following: (1) the increased life-expectancy from 43 to 58 years within the last half century; (2) a better knowledge of the causes of other pulmonary diseases; (3) better diagnostic equipment; (4) increased zeal on the part of the medical profession and laity; (5) a changed attitude on the part of the pathologists in recognizing as primary carcinomata tumours that were once called metastases and sarcomata. The miners of Schneeberg and Joachimstal, are cited as the only evidence of increased incidence due to occupation (alleged radioactive dust).

For a diagnosis the following features are re-emphasized: a gradual appearing cough, followed by a variable but constant pain in the chest, and expectoration frequently streaked with blood, all of which may be accompanied with or followed by dyspnoea. Less reliable and later symptoms are anorexia, fever, loss of weight, aphonia, and dysphagia, limitation of movement of the affected side, decreased breath sounds distal to the bronchial obstruction, hyperresonance above, dullness and ultimately flatness over the tumour, slight or no moisture at first. X-ray: a gradually progressing shadow extending out from the hilus. Bronchoscopy reveals a woody or fixed bronchus, and a biopsy generally clinches the diagnosis. There is scant or mucoid sputum, sometimes streaked with blood, free from acid-fast bacilli; later, tumour cells in the sputum or spinal fluid.

The cases reported are classified according to the various stages of the disease, and divided into three groups for therapeutic possibilities as follows: (1) simple excision of the primary nodule by means of the bronchoscope, followed by radium; (2) lobectomy; (3) palliative.

LEYLAND J. ADAMS

**Cinchophen Hypersensitiveness. A Report of Four Cases and a Review.** Short, C. L. and Bauer, W., *Ann. Int. Med.*, 1933, 6: 1,449.

All four cases developed urticaria following administration of the drug. In one case, attacks of urticaria accompanied by chills and fever were repeatedly produced by repeated administrations of the drug before their cause was realized. Each attack occurred after a shorter interval and with a smaller dose than the preceding one. One case showed an abnormal van den Bergh, and damaged liver function by the Rosenthal test. Prompt cessation of the drug did not prevent the development of the clinical symptoms of acute yellow atrophy two weeks later. Forty-one cases are reviewed. The amount of the drug used before symptoms appeared varied from 1 to 115 grams. The duration of administration was two weeks or less in all but 5 instances. Although urticaria was the



most common type of allergic manifestation to occur, it sometimes took the form of a scarlatini-form, purpuric, morbilliform, vesicular, or bulbous eruption, aphthous ulcers in the mouth, gastro-intestinal symptoms, albuminuria, or syncope with vaso-motor collapse. In 6 cases the allergic manifestations were associated with evidence of liver damage. Their appearance must be considered an indication for the immediate and final withdrawal of cinchophen in all its forms, and the prophylactic administration of glucose for at least one week.

The mechanism of the acquisition of hypersensitiveness from simple non-protein substances, such as cinchophen, is as yet not completely understood. It has been suggested that a secondary allergen is produced in the body by the combination of the drug and tissue protein. The intradermal tests with solutions of cinchophen were on the whole negative.

H. GODFREY BIRD

**Hyperparathyroidism: Its Diagnosis and Exclusion.** Albright, F., *New Eng. J. of Med.*, 1933, 209: 476.

In the healthy adult the serum calcium range is 9.5 to 11.5 mg. and the serum inorganic phosphorus 3.8 to 4.5 mg. per 100 c.c. This constancy is apparently due to the bones. If some calcium and phosphate ions are lost to the fluid system the bones immediately replace them; if some extra ions are added to the fluid system they immediately go to the bones. In hyperparathyroidism the calcium ions are markedly increased and the phosphate ions are decreased. Values of 13 mg. are obtained instead of 10 mg. There is a large outpouring of both of these elements in the urine. This leads to general demineralization of the bones. Secondary changes may be localized. There are four such; deformity, cyst-formation, tumour formation, and fracture. The teeth show no demineralization. Sometimes the teeth become loose and fall out, but the disease process is in the jaws, not in the teeth. Polyuria and polydysia are present in the most cases. Just as hypercalcaemia causes tetany, so the opposite condition leads to sluggishness, decreased muscle tone, constipation and a general depressed feeling.

In the classical type of the disease the diagnosis is usually first suspected by the x-ray man, but the final decision depends on finding a high serum calcium and a low serum phosphorus. The stage just before demineralization is present and before cysts and tumours have appeared is difficult of diagnosis. A patient, aged 60, had been diagnosed as having flat feet, arthritis, neuritis, neurasthenia and ptosis. X-rays showed some demineralization of the skeleton and a distortion of the vertebrae, but no cysts. Her serum calcium and phosphorus values were first found to be normal, but later to be 11.2 mg. and

2.7 mg. respectively. She had a small adenoma of one parathyroid. Therapeutic results were gratifying. Anybody with generalized osteoporosis deserves careful and perhaps repeated studies to rule out an underlying mild hyperparathyroidism before being labeled senile osteoporosis. Many of these patients develop calcium phosphate stones in the urinary passage, and can develop stones without any demonstrable skeletal disease. Every patient with a genito-urinary calculus should be checked up as to the possibility of his having hyperparathyroidism.

Almost any amount of skeletal disease responds to removal of the tumour. The kidney danger hangs over every one of these patients until the tumour is out, and makes all temporizing forms of therapy contraindicated.

LILLIAN A. CHASE

**The Interpretation of Lead Inversion in Bundle-Branch Block.** Nichol, A. D., *Am. Heart J.*, 1933, 9: 72.

This study was made in an attempt to clarify the problem as to which branch is involved in a case of bundle-branch block. The basis of this investigation was that if the left branch of the bundle if His is effected, left ventricular ejection will be retarded owing to a delay in the arrival of the impulse and a longer isometric contraction phase, and therefore the subclavian arterial pulse will begin to rise later in relation to ventricular excitation than if the conducting mechanism were normal. *A priori* if the right branch only is involved left ventricular excitation and contraction will proceed in a normal manner, and ejection, as indicated by the subclavian pulse, should maintain its usual relation to the beginning of ventricular excitation, as indicated by the QRS of the electrocardiogram. In all cases studied an electrocardiogram, the subclavian pulse tracing from the left supraclavicular fossa, and the apical heart sounds were registered simultaneously. In all cases of bundle-branch block, with an upright QRS<sub>1</sub> and downward QRS<sub>2</sub>, the incidence of the subclavian pulse was definitely delayed. It is concluded, therefore, that it would seem probable that this type of electrocardiogram presents a left rather than a right bundle-branch block.

W. H. HATFIELD

**Ulcerative Colitis.** Hardy, T. L. and Bulmer, E., *Brit. M. J.*, 1933, 2: 812.

Ninety-five cases of this disease, treated at the General Hospital, Birmingham, over a twelve year period, are analyzed. Particular attention has been paid to the life history of the disorder and little to questions of etiology. The authors' cases consisted of 48 males and 47 females. The main incidence of the disease seems to fall in the age-period between 21 and 40 years, with the greatest absolute and relative mortality in the third decade. The shortest



duration noted, before a fatal termination, was six weeks, and the longest, 36 years. The mortality during the first year is very high, most of the deaths occurring in cases which show an acute onset. The mortality thereafter diminishes rapidly with every year of survival. Cases with acute onset would appear to be about three times as common as those with an insidious one, and their prognosis is much worse. The least unfavourable cases are those characterized by intermittent attacks with periods of complete freedom. One-third of the patients died during the period under review. The results in the remaining two-thirds are classed as (a) good—where there has been complete restoration to health—19 per cent; (b) fair—complete recovery interrupted by later relapses—18 per cent; (c) moderate—much disability associated with a persistence of obvious symptoms, with or without definite relapses—20 per cent; (d) bad—persistence of symptoms with more or less invalidism—4 per cent. Six per cent had been under observation for too short a period to assess the results. While the type of illness may vary greatly in this disease, from a short, severe illness, suggesting food-poisoning, to a long, insidious one, “yet the clinical features are identical and the one is but a slow-motion picture of the other.”

Treatment of these cases is always “disheartening and confusing.” The authors state that “it is difficult to avoid the cynical conclusion that most cases who get well do so in spite of their treatment.” The general treatment adopted, which they have called, “expectant”, has been prolonged and complete rest in bed, with bland, non-residue diet, with high-calorie and high-vitamin intake; colon lavage with various substances, bland and medicinal; charcoal, china clay and other symptomatic remedies by mouth. In addition to this, 21 patients received polyvalent anti-dysenteric serum. Surgical treatment was used in 25 cases, usually in the more severe and hopeless ones, the procedure being either appendicostomy or cæcostomy. Eight of the surgically treated cases died within 10 days and three survived periods of 6, 8 and 14 months. Good results were obtained in only 12 per cent, but these were admittedly severe cases. The highest proportion of good results (29 per cent) was obtained after serum treatment; only 21 per cent of good results were obtained with expectant treatment alone; but with serum there were more bad and fair results than in the latter group. The death rates were 24 per cent in the serum group and 30 per cent in the expectant group.

No line of treatment, then, seems to be of proved value. In the acute stage, the time-honoured colon lavage may actually do much harm. The basic principles would appear to be absolute and prolonged rest in bed for a minimum of 6 months with a well varied, bland, high-

calorie, high-vitamin diet, the judicious use of opiates and the provision of adequate fluid by mouth, rectum or, if necessary, intravenously. Recovery in this disease is invariably slow and rarely complete. There are few diseases, however, in which the patient can reach such a state of emaciation and yet recover.

W. FORD CONNELL

## Surgery

### The Results of Gastroscopy. Gutzeit, K., *Med. Klinik*, 1933, 29: 965, and 1,000.

At the author's clinic in Breslau 4,000 gastroscopies, of which he himself did 1,200, have been carried out without an accident. Flat ulcers, erosions, and a large number of inflammatory gastric mucous membrane changes, as well as total mucous membrane atrophy, which are all easily recognized by gastroscopy, cannot be demonstrated roentgenologically. The gastroscope is very useful in recognizing early lesions, particularly in the upper end of the stomach.

The following are the chief points in his summary. (1) Chronic gastritis is the most frequent cause of gastric complaints. It was found in over 90 per cent of patients with gastric symptoms. (2) The symptoms of gastritis may simulate almost any abdominal condition. Atrophic gastritis can lead to great loss of weight and simulate the clinical picture of carcinoma. (3) In gastritis, we may find hyper-, normal, or anacidity. Increased mucus secretion is part of the characteristic picture, but may be absent. (4) Erosions and ulcers without an accompanying gastritis do not exist. The author has found gastric ulcers in cases with achylia (even after histamine) and even in pernicious anæmia. The author has never seen a deep ulcer develop from the superficial mucous membrane defects or erosions. No matter how soon after the appearance of symptoms gastroscopy has been done, either superficial erosions or fully developed deep ulcers, or both, were found. So the author believes that the deep gastric ulcers are caused by a disease process within the wall of the stomach, and their depth is determined by the depth of the lesion in the stomach wall. (5) A chronic dyspepsia with eructations of gas and belching does not exist without a gastritis. (6) “Gastric neuroses” in the majority of cases have been found to be due to gastritis. (7) Occult bleeding may also be due to gastritis. (8) The author found the majority of cases of pyrosis to have an œsophagitis of the lower œsophagus. He has seen this clear up when the symptoms of pyrosis disappeared.

In the second paper the differential diagnosis of the more common conditions is discussed. Gastric ulcer has a sharply-cut margin and a more or less pronounced marginal swell-

ing which may exaggerate the depth of the ulcer in the x-ray, and a decrease in this swelling may give the impression that the ulcer has healed. With endoscopy one sees that a disappearance of the niche does not necessarily mean that the ulcer has healed. The symptoms also disappear with the marginal swelling, but the ulcer is present often for months after this. Diverticula do not contain any secretion in their base and normal folds of mucous membrane can be seen running into them. The serious post-operative complaints following gastro-enterostomy have been found to be due to a severe gastritis and usually not to marginal ulcers. It has been found that even deep ulcers may heal with medical treatment.

Fibromas have a smooth transparent glassy surface and are often found in cases of gastritis. Adenomas show an evenly granulated surface without ulceration and an evenly distributed circulation. They usually sit on an elastic, non-irritated, non-infiltrated mucous membrane, as distinguished from carcinoma, which is either pale or deep bluish-red in colour and has an irregularly infiltrated base with a complete change of the normal mucous membrane folds, so that the tumour may be bleeding and partly covered with a glassy necrotic material.

By continuous correlation of x-ray, gastroscopic, and clinical findings, the author has come to the conclusion that diseases of the gastric mucosa, gall bladder or appendix, in the majority of cases, are only localized exaggerated effects of a general gastro-enterocolitis.

JOACHIM BRABANDER

**Cancer of the Colon.** Wilkie, D. P. D., *The Lancet*, 1934, 1: 65.

In this article Wilkie reports 181 cases of carcinoma of the colon. In 101 cases a radical operation was performed: 74 were in the distal colon and 27 in the proximal colon. He very definitely divides his cæcal carcinomas from those of the ascending colon, the division being at the ileo-colic junction. In 3 cases he explored the abdomen in the face of a negative barium enema, to find an annular carcinoma. He thinks that the combination of barium and air enemas is of value. In the operative treatment one must realize that every patient with a growth in the colon is suffering from a potential, if not an actual, intestinal obstruction, and that the condition of the bowel wall and the general condition of the patient are unfavourable for successful surgery. He states that the simplest, but not necessarily the best, method of draining the bowel, is by a blind cæcostomy. He believes that an immediate resection, with the introduction of a Paul's tube into each cut end, is permissible when the obstruction has not been complete. He believes that there should be an interval of weeks, not days, between the drain-

ing of the bowel and the resection. He immunizes his patients against *B. coli* and streptococcus before operation, but he thinks that leakage from the suture line is a more real and more serious danger, and that the success of an anastomosis depends on lack of tension. In the transverse and descending colon he always divides the phrenico-colic ligament. If he does an end-to-end anastomosis he divides the tæniæ, to get rid of the sacculations and equalize the tension at all points in the circumference of the bowel, and advises that some drainage of the bowel, preferably by a cæcostomy, be done. He does not believe that extension by contiguity prevents a successful removal. He has had 15 deaths in the 101 cases of resection, 2 of which were due to a post-operative peritonitis. In 38 cases a primary resection was done, with a mortality of 13 per cent. In 30 cases a preliminary drainage had been done with 3 deaths: 41 cases of the 101 reported were alive after three years. In his summary he recommends preliminary drainage, and avoidance of tension on the suture line, and states that spread by contiguity to adjacent organs is not a bar to radical surgery, and that the end-results are encouraging.

W. L. GRAHAM

**Diagnosis and Treatment of Fractured Skulls.**

Wright, L. T., *et al.*, *Arch. Surg.*, 1933, 27: 878.

The authors report their experiences in the study and management of 347 consecutive cases of cranial and intracranial injuries, at the Harlem Hospital, New York. With a history of trauma, blood in the spinal fluid was the basis of the diagnosis of intracranial injury in patient who lived and an autopsy in fatal cases. Erythrocytes in the spinal fluid are the most trustworthy evidence of injury that is available at the present time. The incidence of actual fractured skulls is much higher than the incidence of intracranial injuries without fracture of the skull, while the mortality from the latter is only about one-third the mortality from the former. The great majority of the patients in the authors' series of fractured skull, sustained this injury in automobile accidents. Thirty-eight of the 73 patients died within 12 hours after admission to the hospital. Death after 48 hours was in most instances due not to cerebral laceration but to certain complications, such as meningitis, hypostatic pneumonia, associated injury or exhaustion and inanition. Death due to laceration of the brain and subdural hæmorrhage usually occurs within forty-eight hours after the injury.

Cerebral concussion, denoting the unconsciousness which occurs after an injury to the head, is not usually associated with fracture of the skull in the clinical acceptance of the word. The term has a somewhat doubtful pathological basis, and if it is to continue in use, Trotter's



description of the clinical features should be adopted, which are (1) instantaneous onset, (2) paralytic nature of the symptoms and (3) a tendency to disappear spontaneously, and Wright and his associates would add (4) a history of trauma and (5) the elimination of alcohol and drugs and other diseases.

Laceration of the brain has been the most common pathological finding, with or without marked hæmorrhage, in all cases of severe trauma, and the spinal fluid is bloody. It may occur at the point of injury or may be contrecoup, which is more frequent.

Bleeding from one or both ears is a rather reliable sign of fractured skull. The escape of spinal fluid from the ear makes the diagnosis of fracture of the skull certain. Vomiting was observed only eleven times in the series. Urinary incontinence was noted in more than fifty patients and its occurrence in patients not under the influence of alcohol, is of grave prognostic significance.

The authors used conservative non-operative treatment with rest in bed, good nursing and the maintenance of nutrition. The patient was kept warm and suction was used to keep the throat clear of mucus. Operations were performed in all cases of compound depressed fractures, in some of simple depressed fractures, and in those with epidural or suspected epidural hæmorrhage. No operation was performed for cerebral compression.

G. E. LEARMONTH

### Obstetrics and Gynæcology

**Diabetes Mellitus and Pregnancy.** Skipper, E., *Quart. J. of Med.*, 1933, 2: 353.

The successful management of diabetes mellitus during pregnancy is often difficult and necessitates a familiarity with the influence of gestation upon the disease. This review, accordingly, of 33 personally observed cases, with 118 cases collected from the literature is most helpful. It would seem that while insulin has considerably improved the outlook for the mother, fetal mortality is still very high—in the vicinity of 40 per cent. It appears certain that insulin increases the fertility of the diabetic. During the latter part of pregnancy, there is usually a lowering of glucose tolerance, though uncommonly the reverse may be the case (there are no grounds however for believing that such rise in tolerance is due to the transfer of fetal insulin to the mother). After childbirth, a gain in tolerance, the metabolism returning to its pre-gestation condition, is to be expected. Hypoglycæmia, then, in patients receiving insulin, is a definite danger during the puerperium. With adequate treatment, pregnancy should have no harmful effect on the diabetic. Occasionally a lowered renal threshold is found, rising to normal after de-

livery. This makes control by urinalyses alone difficult. There appears to be more danger of ketosis in pregnant than in non-pregnant diabetics.

The most important cause of fetal mortality is poor control of the maternal disease during the latter months. Other causes are fetal over-development and congenital abnormalities. Hydramnios is an occasional source of danger. It is only by constant supervision and rigid blood sugar control of the mother during pregnancy that a living child can be assured. The occurrence of fatal hypoglycæmia in the child after birth, associated with hypertrophy of the islands of Langerhans has never been proved. The child of a diabetic is not particularly liable to develop the disease. Since diabetes may develop during pregnancy, all cases showing sugar in the urine should be carefully investigated to exclude the possibility of this disease.

The author finds that no increase of diet is necessary during pregnancy, since the caloric requirements are only 4 per cent higher. He uses a diet with a little more than 1 gram of protein per kg. of body weight, 120 to 140 grams of carbohydrate and about 100 grams of fat. The urine and blood sugar are checked at least fortnightly and the patient admitted to hospital for a short observation period every two months. Cæsarean section is only indicated when the size of the child is excessive. Breast-feeding should be allowed if possible. Sterilization of a diabetic is only advisable if the patient's mentality is such that her cooperation during further pregnancies is unlikely. It may also be necessary in severe diabetics who have been found difficult to control at the first pregnancy.

W. FORD CONNELL

**Diagnosis and Treatment of Benign and Malignant Lesions of the Uterine Body.** Neill, W., Jr., *Virginia Med. Monthly*, 1933, 60: 293.

It is now generally recognized, in cases of uterine fibroids requiring treatment, that both surgery and irradiation are effective procedures. Operation is indicated in, (1) large rapidly growing fibroids; (2) in large tumours associated with pain; (3) in tumours accompanied by inflammatory changes; (4) in tumours accompanied by malignancy of the body (sarcomatous degeneration is extremely rare, but the author has observed 12 body cancers in a series of 1,500 fibroid cases). (5) in impacted tumours interfering with the urinary function; (6) in calcified tumours with active symptoms; (7) in cases where after expert examination, there is a doubtful diagnosis; and (8) in patients possessing a radiation "phobia." Irradiation is indicated (1) in all tumours with hæmorrhage, from small nodules up to freely movable growths reaching as high as the umbilicus; (2) in selected cases,



even larger tumours; (3) in the operative group, where there is a contraindication for surgery. Irradiation will control hæmorrhage, reduce the size of the tumour and in most cases cause its complete disappearance. In young patients there may be a recurrence of menstruation and subsequent child-birth. If submucous fibroids are present they should be removed by vaginal myomectomy. Irradiation treatment consists in delivering an intra-uterine dosage of 1,000 milligram hours. An external x-ray dosage through two pelvic portals, one-half an erythema dose to each area, completes the treatment. An immediate cessation of hæmorrhage may be expected in 50 per cent of the cases; there may be one to four menstrual periods after treatment. Accompanying the artificial menopause there may be vasomotor disturbances, but in the vast majority these are less pronounced than in the case of spontaneous cessation. In none of the 1,500 cases observed was malignant degeneration seen. No deaths could be attributed to the treatment.

Taking an average of all hysterectomies for fibroid growths, there is an immediate mortality of 5 per cent, and the possibility of major post-operative complications is not negligible. Besides this there is a disagreeable hospital experience and the patient is unable to assume routine duties for a very indefinite period; this coupled with the indictment that it is after all a mutilating operation tends to make some better form of treatment advisable. During the past fifteen years leading gynaecologists have been prescribing irradiation and favourable results have increasingly obtained in proportion as better selection and improved technique have obtained. While malignancy is not a common accompaniment of fibroids, in all cases in which there is abnormal uterine bleeding, leucorrhœa, or watery discharge, it is most important to eliminate malignancy. It is impossible to place too much emphasis on the importance of early curettage and microscopic study of the tissue removed. In many clinics the grade of the tumour determines the type of treatment. Until the last decade the universally accepted treatment was complete hysterectomy. Recently, various workers have reported results in treating early cases of cancer of the body of the uterus by irradiations; in these reports it is shown that the five-year cure rate equals that obtained by surgery. In the higher grades of malignancy, cure is not to be expected, and, as they are highly sensitive tumours, radiation is to be preferred to surgery. In operable cases, radiation alone offers a method of treatment far better than we have before realized. It obviates a primary mortality and is to be recommended in all bad surgical risks.

E. E. SHEPLEY

## Pathology and Experimental Medicine

**Studies on the Etiology of Blood Diseases: A pathological agent in normal human bone marrow.** Friedemann, U. and Elkeles, A., *Brit. M. J.*, 1933, 2: 1,110.

The authors present some interesting results following the injection of normal and pathological bone marrow into normal rabbits. These results were the same whether normal marrow or marrow from cases of leukæmia or pernicious anæmia was used, namely, following the injection of 0.3 c.c. of emulsified marrow through the atlanto-occipital membrane, either paresis of the hind limbs or spasmodic contraction of the neck muscles appeared, and in most cases there was steady downward progression to death. In the cases considered in the report, all inocula were sterile on culture. Rabbit to rabbit inoculation of the experimentally produced encephalitis was attempted but met with indifferent success. Post-mortem examination of the affected rabbits showed striking changes in the liver in all cases, the cells being large and foamy and packed with glycogen. The spleen in all cases showed marked hæmosiderosis. The findings in the brain are, remarkably, not noted.

The authors feel that they have successfully demonstrated in normal human bone marrow the presence of an agent pathogenic for rabbits, which causes an encephalitis if injected intrathecally. They feel that there is not sufficient proof that they are dealing with a living virus. That the virus of Kling, normally present in a certain percentage of rabbits, is not the cause of the encephalitis, would seem to be shown by the great regularity with which the intrathecal inoculations were followed by encephalitis. The similarity of these results to those of Gordon, using lymphadenomatous glands, is pointed out. The picture produced in his rabbits was not identical and Gordon was quite unable to transmit his encephalitis from rabbit to rabbit. It remains to be seen whether there is any close connection between these two experimentally produced types of encephalitis.

W. FORD CONNELL

**Hereditary Gaucher's Disease.** Anderson, J. P., *J. Am. M. Ass.*, 1933, 101: 979.

Gaucher's disease is due to a disturbed lipid metabolism with the production of an abnormal substance, kersin, which is stored in the reticulo-endothelium, thus giving rise to the Gaucher cell. This is found in all organs where there is the reticulo-endothelial cell, especially in the liver, spleen and lymph nodes. It is characterized clinically by enlargement of the liver and spleen, pigmentation of the skin, pinguecula-like thickenings of the conjunctiva, hæmorrhagic diathesis, leukopenia, and anæmia.

Anderson reports a family in which there were probably 8 cases in the first and third generation, with a clear second generation. The paternal grandmother and her two sisters had enlarged abdomens and yellowish brown skin. It was stated that all three died of the same cause. These were probable cases of Gaucher's disease. The father, son of this woman, was supposedly normal, as were his brother and sister. The woman he married had no evidence of Gaucher's disease. Nine children were born to this couple, the three men living and well, with no signs of Gaucher's at the ages of 41, 26 and 19. Of the six girls in the family, one died at 1½ year of measles; one died at 6 years with a very enlarged abdomen and yellowish discoloration of the skin. One died at 17 years; she had had an enlarged abdomen, greenish yellow skin. Her spleen was removed and the pathological diagnosis was Gaucher's disease. She died three months later of extensive pulmonary tuberculosis. (This is of interest because of the report by Beckman and Jäderholm that tuberculosis is more prevalent in persons with their spleens removed than would be expected on the basis of the general incidence of tuberculosis). A fourth sister, aged 24, has no splenic enlargement, but has a distinct yellowish discoloration of the skin. A fifth sister, aged 21 has the skin discoloration, a spleen that is two inches below the costal margin, a liver that is palpable on deep inspiration, a history of frequent nose-bleeding, a mild anæmia, and leukopenia, with the granulocytes showing marked reduction. She refused to have a splenic puncture done. The sixth sister, aged 33, has an enlarged spleen and liver, the former being well below the umbilicus, the liver one inch below the costal margin. Gaucher cells were present on splenic puncture. The skin was discoloured as in the other sisters; there was a mild anæmia, a leukopenia, pinguecula-like thickenings on the conjunctiva; nose-bleeding was frequent; uterine hæmorrhage occurred in the intermenstrual period. There was a progressive increase in the size of the spleen and the liver while the patient was under observation; the anæmia and leukopenia became more marked in spite of liver therapy. Her one son, aged 12, was so far normal.

MADGE THURLOW MACKLIN

**Erythema Nodosum.** Collis, W. R. F., *Brit. M. J.*, 1933, 2: 1,163.

In 1931, the author first propounded the view that erythema nodosum was a hyperactive tissue-response to any of several bacterial allergens, commonly either tuberculin or the hæmolytic streptococcus endotoxin. Subsequent investigation has shown that tuberculous cases are by far the commonest, even in London, where streptococcal infections of all types are common. Of 38 London cases investigated, 71

per cent were definitely tuberculous, 18.4 per cent streptococcal, and 10.6 per cent "indefinite". Of 10 Dublin cases, 9 were tuberculous, 1 streptococcal. An occasional case can be shown to be due to other allergens, as the meningococcus, *B. coli*, etc. Investigation of the cases cited seems to have been thorough. The author does not give many ages, but it would appear that most of his cases have been in young children; such streptococcal cases as are quoted in any detail are in older children or adults.

W. FORD CONNELL

**The Value of Alimentary Galactosuria in the Diagnosis of Jaundice.** Tumen, H. J. and Piersol, G. M., *Ann. Int. Med.*, 1933, 7: 311.

The use of galactose as a test for liver function is based on ample theoretical data. Galactose is utilized exclusively by the liver, is not utilized in liverless animals, is without a kidney threshold and its metabolism is uninfluenced by insulin, even in toxic doses. The authors report their observations on the use of galactose in 40 gram doses, in 54 cases of jaundice. A positive test is considered by the authors to be one in which more than a total of 3 grams of galactose is excreted. Doubtfully positive cases are those in which between 2 and 3 grams are excreted, and negative cases are those in which less than 2 grams are excreted. Owing to the various factors influencing the blood sugar curves following the ingestion of galactose, and owing to the fact that normal curves have been found in cases with severe galactosuria, and in which there is extensive liver damage, the authors have relied solely on the examination of the urine. In their 54 cases, 18 had obstructive jaundice, 23 had catarrhal jaundice, and 13 had toxic hepatitis. These cases showed respectively 5.5, 78.3 and 54 per cent of positive tests.

They conclude that a positive test is obtained in all cases of actual hepato-cellular damage in which there has not been time for regeneration of liver cells sufficient to handle the excess galactose. Cases of catarrhal jaundice with negative results are believed to be cases where the inflammation is in the ducts, giving rise to an obstructive jaundice.

E. S. BIRD

**Cerebral Birth Conditions with Special Reference to the Factor of Hæmorrhage.** Patten, C. A. and Alpers, B. J., *Am. J. Psychiat.*, 1933, 12: 751.

This study was made on 30 infants' brains removed routinely at autopsy, regardless of any indications before death that there were cerebral complications. Seventeen of them showed subarachnoid hæmorrhage, and 26 showed subependymal lesions. Of the 17 who had subarachnoid lesions 9 were instrumentally delivered, and 2



others by Cæsarian sections. Seven were full term; 4 were eight-months, 4 were seven-months and 2 were six-months babies. The duration of labour, the type of presentation, the amount of anæsthetic or its type, and the instrumentation all seemed to play no rôle in causing the hæmorrhage or increasing its extent. The general condition of these infants was "poor" at birth, and the inference drawn from this study was that the hæmorrhages were prenatal, and were not caused by any environmental factor such as trauma received at birth. The exact cause is difficult to state; perhaps it was defective myelinogenesis. This study is of interest to the student of heredity of mental defect, which is so often attributed to long and difficult or instrumental delivery by both parents and physician. Many of these so-called birth-injury cases may be merely the expression of defective constitution which revealed itself in cerebral hæmorrhages and defective mentality.

MADGE THURLOW MACKLIN

### Therapeutics

#### A New Treatment of Osteomyelitis. Stewart, M. A., *Surg., Gyn. & Obst.*, 1934, 58: 155.

This is the report of experiments to determine how maggots do effect a cure in cases of osteomyelitis.

During one stage of the investigation it was found that the maggots (*Lucilia sericata* Meig) exude calcium carbonate through their body walls, a very important finding, since it has been pointed out before (Beckhold, 1929) that calcium carbonate stimulates phagocytosis. It has also been known for some time that the bacteria excrete a leucocidin, which, unless removed or rendered inert, kills off the leucocytes as rapidly as they are attracted to the focus of infection. It has been previously supposed that the maggots cared for this exotoxin given off by the bacteria by absorbing it and rendering it non-toxic in their bodies through digestive processes. In order, then, to produce a chemical substitute for living maggots, two steps were necessary, viz., (1) suitable introduction into the wound of a form of calcium carbonate, in order to stimulate phagocytosis, and (2) a chemical means of removal from the focus of the accumulated leucocidin, a substance recognized as hampering phagocytosis. After prolonged experimentation on animals it was found that the leucocidin can be successfully rendered inert by exposure to a dilute aqueous solution of picric acid, while the calcium carbonate may be introduced in the form of an aqueous suspension. The author then reports in detail work carried out on 41 cases of osteomyelitis, mostly of the long bones of arms and legs, in patients of varying ages from 6 to 60; some of these patient had suffered for 15 to 20 years and undergone several

operations and different types of post-operative treatment during that period. Either a complete disappearance of the infection or a definitely improved condition is reported in practically every case.

Briefly, the treatment consists of the following steps. After an operation, when the necrotic bone is removed surgically, the wound is packed for 24 hours with vaseline gauze in order to allow the trauma to subside; at the end of this period the gauze packing is removed and the wound is thoroughly irrigated with the picric acid solution (0.25 per cent aqueous solution of picric acid to which 8 per cent glycerine has been added) by means of a syringe. Within a few seconds' time an aqueous suspension of calcium carbonate (20 grams of calcium carbonate to 215 c.c. of distilled water) is sprayed into the wound by means of a nasal atomizer, until a thin layer of a white precipitate of calcium picrate is laid down over the osseous and soft tissues. The author suggests that these treatments be carried out three times a week, unless the condition is very acute, when daily dressings are recommended.

B. BRACHMAN

#### The Oral Administration of Iron in Hypochromic Anæmia. Heath, C. W., *Arch. Int. Med.*, 1933, 51: 459.

The author analyzed 84 cases of hypochromic anæmia due to various causes, selected from a large group of patients with different forms of anæmia who have been carefully studied in the Thorndike Memorial Laboratory during the last four years. Many of the cases had a multiple etiology, for example, poor diet associated with chronic loss of blood from peptic ulcer, or idiopathic hypochromic anæmia with achlorhydria and chronic menorrhagia. There were also included two cases of cancer of the stomach with achlorhydria, one of Hodgkin's disease, and one of amœbic dysentery, in all of which there had been a pronounced chronic loss of blood. The author emphasizes the difference between acute blood loss with a good hæmoglobin-building reserve and chronic blood loss with inadequate diet and depleted stores of hæmoglobin-building material. The reticulocyte response has been shown to be a reliable laboratory test for the effectiveness of iron therapy in different kinds of anæmia. In the clinical investigation of iron therapy in hypochromic anæmia he states the two factors of primary importance are: first, the selection of suitable cases with regard to their type and etiology and the absence of complications, and second, the establishment of adequate control periods.

He describes an arbitrary test whereby the hæmopoietic response to iron may be judged quantitatively, and the adequacy of the dosage of iron determined. This is done by comparing the reticulocyte response and the rate of hæmo-



globin rise after iron to certain standards. He also describes a comparative test whereby several preparations of iron may be compared with one another as to potency.

To be certain of giving adequate amounts of iron in hypochromic anæmia, he advises giving large doses, such as 6 grm. (90 grains) of iron and ammonium citrate daily, corresponding to 1 grm. of metallic iron. In discussing the influence of the addition of copper to iron he states that it is inadvisable to give copper salts as a routine measure in hypochromic anæmia in adults.

L. J. ADAMS

**Artificial Pneumothorax Treatment.** Jessel, G., *The Lancet*, 1933, 225: 1360.

The author discusses the results of artificial pneumothorax treatment of pulmonary tuberculosis in 139 male patients of from 15 to 55 years. These cases were all drawn from one small area of 345,000 people and were all treated by one man. From his statistical results the author draws the following conclusions. Practically, the use of pneumothorax is limited. It should not be used in severe bilateral cases and in cases with marked adhesions. Cases with marked fibrosis and of middle age are apt to be made worse by pneumothorax. The most suitable case for an artificial pneumothorax is a recent unilateral case with comparatively slight involvement of the opposite lung. Small frequent refills are preferable to large infrequent ones. Cases in which collapse cannot be induced by artificial pneumothorax may show good results with a phrenicectomy, and pneumothorax should always be considered as one form of collapse therapy which may in some cases be less useful than other forms. The results of artificial pneumothorax are a restoration to working capacity and disappearance of tubercle bacilli from the sputum in a great many cases. The benefits of this treatment are thus not limited to the patient but have an important bearing on prevention.

GUY H. FISK

**Treatment of Chorea by Induced Pyrexia.** Cheetham, J. W., *Brit. M. J.*, 1933, 2: 815.

The author presents the results he has obtained in 4 cases of Sydenham's chorea, treated by Sutton's method of induced pyrexia, using injections of T.A.B. vaccine daily for 7 to 10 days. The initial dose was 0.1 c.c. intravenously, and each successive dose was doubled, if the preceding reaction had not been too severe. Vomiting and cyanosis were usually observed after the initial injection, and the choreic movements were for a time increased. The final injection was usually found to produce no reaction, apart from the pyrexia, which was usually from 103 to 106°. The author has paid particular attention to the cardiac aspect of the

disease and the effect of the treatment on the heart.

The first case quoted had no cardiac complications and never developed any, while the attack had subsided dramatically by the time the treatment was concluded, although the case was one of moderate severity. In Case 2, two courses of treatment were necessary before the movements subsided—six weeks after the onset of the attack. Case 3 was observed during two attacks of chorea, for the first of which she was given a course of injections. After this, there were no evident signs of chorea for three months, when she had a recurrence and was readmitted, the movements this time without injections, requiring two months to disappear. There was no heart involvement. Patient 4 had advanced rheumatic carditis when chorea developed. He was given injections and within seven days the choreic movements were no longer evident. Within five months, however, he was back in hospital with severe chorea and acute pericarditis which proved rapidly fatal. It would appear possible, then, that the treatment had accelerated the fatal result. It certainly had no beneficial effect on the carditis.

The author concludes that artificial pyrexia appears to shorten the duration of choreic movements, but does not prevent recurrence; moreover, it has no beneficial effect on carditis and indeed may aggravate it. The great danger of the treatment lies in this aspect—that it may abolish the movements and produce a false impression of cure, while all the time changes may be occurring in the heart. This method of treatment then, requires much more exhaustive trial before it could be generally adopted, and would seem to have a very limited place in treatment.

W. FORD CONNELL

## Urology

**Injury to the Bladder after Irradiation of the Uterus.** Dean, A. L., *J. Urol.*, 1933, 29: 559.

Forty-seven patients have been treated for vesical injuries after irradiation of the uterus. Both radium and x-rays had been used, though by far the most intense radiation was with radium. The radiation therapy varied within wide limits, and on the average preceded the onset of bladder symptoms by 2½ years. These consisted of frequency, dysuria and hæmaturia. The onset was sudden and the suffering intense; in some there was extensive destruction or even death. Cystoscopic examination showed ulceration, anæmic areas surrounded by intense inflammation, or punctate hæmorrhage. The lesion was situated on the posterior third of the base in or near mid-line. Diagnosis was based on the history, vaginal examination, the cystoscopic picture, and a biopsy. Treatment consisted of Tr. Hyoseyami and codein for pain, dilute

phosphoric acid, both by mouth and by lavage, and instillations of argyrol and mercurochrome.

When one employs the accepted methods of treating carcinoma of the uterus with high voltage rays combined with radium within the cervix or corpus the bladder base must in some cases receive sufficient radiation to cause ulceration. This possibility must be recognized by all who treat uterine cancer, as injury may even follow light radiation to relative insignificant diseases. All women of cancer age who suffer from frequency, dysuria, and hæmaturia with ulceration of the bladder should be questioned as to the possibility of a tertiary radiation reaction. In addition to cystoscopy, a vaginal examination and biopsy should be performed in all cases.

With proper management the end results are excellent, but healing is often slow. If such a radiation injury is treated by radiation, cauterization or other destructive methods results are disastrous.

N. E. BERRY

### Ophthalmology

#### Specific Treatment of Ophthalmic Tuberculosis with a new Tuberculosis Vaccine "AO".

Nakamura, B., *Arch. Ophth.*, 1933, 10: 161.

Tuberculosis vaccine AO is a preparation of tubercle bacilli originated by Arima, Aoyama and Ohnawa in Osaka, Japan, and licensed by the Japanese government in 1927. According to the originators, AO is made from tubercle bacilli of the human type. It is sterile, consists of the native protoplasm of the bacilli, is easily absorbed, is completely innocuous, is derived from strongly immunizing strains of bacilli, and has a uniform potency. It is sterile and there is no danger of infection. As it consists of the native protoplasm of the bacilli, it is able to immunize the inoculated organism in the same way as the organism is immunized by infection with live tubercle bacilli. As it is easily absorbed, it acts quickly as an antigen by causing the production of antibodies in the inoculated organism. The easy absorbability is brought about by the autolytic changes which, during the long cultivation, take place in the bacilli, which are devoid of waxy substances. AO is innocuous, as its use in 400,000 patients in different parts of the world up to the end of 1932 shows. No ill effects have resulted from its administration up to the time of writing. Because this vaccine consists of specially selected, strongly immunizing, strains of bacilli, it is remarkably effective. Its potency is constant, as its efficacy is measured by a special immunobiologic method and is expressed in antigen units (AE). The application of AO is threefold; it may be used for prophylaxis, diagnosis and therapy.

S. HANFORD MCKEE

#### Tumours Affecting the Optic Chiasm and Optic Tracts. Globus, J. H., *Arch. Ophth.*, 1933, 9: 729.

There are several diseases of the central nervous system in which visual disturbances are frequent. Chief among them are epidemic encephalitis, multiple sclerosis, various forms of syphilis of the nervous system, and above all, intracranial tumours. Some form of visual disturbance, such as diplopia or blurred vision, may be the earliest symptom complained of by the patient, and for this reason the ophthalmologist is often the first to be consulted in the belief that the visual defect is due to some isolated and focal disease of the eye. However, helpful as the information obtained from the study of the eye grounds may be, the results obtained from the study of the acuity and the fields of vision in instances in which the tumour has encroached on some part of the optic system are of a still more appreciable value. Disturbances in acuity of vision and particularly in the fields of vision are common in tumour of the brain and are, perhaps, more frequent than is commonly recognized. Unfortunately, there seems to be still some laxity as to the frequency and the precision with which visual fields are studied and scotomas outlined.

Tumours restricted to the chiasm are exceedingly rare. Tumour of the craniopharyngeal duct is another form of suprasellar tumour which symptomatologically is closely related to the type just mentioned. The typical case presents a characteristic array of signs and symptoms which in common with ophthalmological and roentgenological findings, make the diagnosis rather simple. Suprasellar meningioma is another not infrequent parachiasmal lesion which at times is clinically indistinguishable from the forms already described. The pituitary adenoma is too well known to be considered at length, but attention should be called to the frequent deviations from the characteristic clinical picture which are not so fully appreciated. Lesions of the temporal lobe when not accompanied by such localizing signs as uncinat seizures, visual hallucinations, or typical speech disturbances, often serve as a severe test of diagnostic ability. The most characteristic sign of a tumour of the occipital lobe is the homonymous hemianopia particularly when it is an isolated finding. Alone, however it would be insufficient to place the lesion with certainty in this region, as homonymous visual defect, as already shown, is a frequent finding also in tumours of the temporal lobe.

S. HANFORD MCKEE



## Neurology and Psychiatry

**Psychotherapy in Private Practice.** Thom, D. A., *Am. J. Psychiat.*, 1933, 13: 1.

The author emphasizes the present controversial state of psychotherapy. Psychoanalysis, hypnosis, suggestion, etc., each have their advocates and each their critics. There must be adequate consideration of physiologic factors, and it must clearly be recognized that the physiological and the purely psychological approaches are mutually complementary and not (as is sometimes held) opposing methods. In this connection the author very pertinently points out that the extreme stands taken by some protagonists of the various schools suggests a lack of recognition of the emotional factors influencing that individual psychiatrist's viewpoint.

The particular type of psychotherapy selected must be dictated by the needs of the patient in question. The factor influencing the choice of method are catalogued under six main heads.

(1) *The patient*.—Intelligent patient offended by crude suggestion: others incapable of appreciating an analytic approach. (2) *Nature of symptoms*.—Certain symptoms must be removed by crude suggestion before any attempt at more adequate therapy can be attempted. (3) *Conditions under which symptoms were acquired*.—In those neuroses occurring abruptly in persons of mediocre ability where the symptoms (generally physical) represent a very immature method of reacting to a difficulty, the author feels that suggestion should be used to clear up the symptoms and then the inevitable residuum approached by an attempt at re-education. In the true anxiety states however, which are insidious in onset and attributable to factors far in the past suggestion is really valueless.

(4) *Purpose which neurosis serves*.—The question "What purpose does the neurosis serve in the life of the individual?" is without doubt the most important challenge which the psychiatrist must answer. There is a very real correlation between the ability of the psychiatrist to answer this question and the success of his psychotherapy. In this connection Dr. Thom wisely points out that many of our patients' conflicts are more superficial and accessible than is generally thought. As he pithily puts it there is danger of dragging the bottom when the fish are at the surface.

(5) Whether precipitating cause continues to operate. (6) The method in which psychiatrist has most confidence.

In conclusion, in private practice the type of psychotherapy should be selected on the needs of the individual case, basing one's consideration on the foregoing schemes. If the particular case requires psychotherapy of a type one is not competent to administer then the patient

must be referred to some better qualified individual. This surely is the attitude of most of us who profess to be practising psychiatry in what we believe to be an ethical way.

G. N. PATERSON-SMYTH

**Verified Tumour of the Temporal Lobe.** Rowe, S. N., *Arch. Neurol. & Psychiat.*, 1933, 30: 824.

The temporal lobes are more or less silent areas. As a rule the patient with a temporal lobe tumour only becomes aware of his disease with the advent of increased intracranial pressure. Mental abnormalities of varying forms are quite frequent and are probably due to the increased pressure; 36 per cent of the 52 cases reviewed by Rowe suffered from convulsive seizures. Three of the recognized symptoms of damage to the cortex of the temporal lobe—aphasia, uncinat attacks, and dreamy states—did not occur in a high percentage of the cases in this series. Aphasia was found in one-third of the patients with tumours on the left side. The accurate determination of the visual fields is of great importance. The finding of a homonymous hemianopia in conjunction with other neighbourhood signs makes the diagnosis certain. Signs of involvement of the adjacent Rolandic area were found in 50 per cent of the cases. In the cases in which the lesion is situated at the base of the lobe pressure on the fifth or the third nerve occurs relatively frequently.

FRANK A. TURNBULL

**Hæmorrhage into Gliomas.** Oldberg, E., *Arch. Neurol. & Psychiat.*, 1933, 30: 1061.

Contrary to a widespread belief, hæmorrhage into a glioma is a relatively uncommon phenomenon. Spontaneous massive hæmorrhage occurred in 31, or 3.7 per cent, of 832 cases of glioma observed in Dr. Harvey Cushing's clinic. The hæmorrhage was accompanied by appropriate clinical symptoms in less than 1 per cent of the series. The same type of symptoms may also appear in patients with tumours in which there has been no hæmorrhage. Occlusion of cerebral vessels, shutting off of the foramen of Munro or aqueduct of Sylvius, or acute œdema, are more likely causes of sudden acute disturbances. Only a very dubious diagnosis of hæmorrhage into a glioma in the presence of the sudden onset or acute exacerbation of symptoms of tumour of the brain can be made. Contraindications to operation should not be based on such an assumption because of the comparative rarity of the condition, because of the reasonable doubt in its diagnosis, and because there is no evidence that operation is unduly hazardous in these cases.

FRANK A. TURNBULL



## Obituaries

**Dr. Louis de Lotbinière Harwood** died suddenly on May 15, 1934, at his home in Montreal. He was 68 years old. Dr. Harwood's reputation as an educationist and as a surgeon extended over the whole North American Continent as well as to Europe.

Dr. Harwood was born at Vaudreuil, Que., on April 27, 1866, the son of Henry S. Harwood, C.E., a scion of an ancient and noble French family.

His educational career commenced at the College at St. Thérèse, after which he went to Rigaud, and attended the large seminary at that place. In 1886 he commenced his medical studies at Laval and received his degree in 1890.

In 1894 he went to Europe to take a course of advanced studies, paying particular attention to gynaecology. While in France he had the opportunity of studying under Dr. Pozzi, the most famous gynaecologist in the French Republic, and was for a time his assistant. Returning to this country in 1896, he was appointed assistant gynaecologist at Notre Dame Hospital. Upon the death of Dr. Brennan, in 1903, he became head gynaecologist at Notre Dame. He was one of the promoters of the conference of French-speaking members of the medical profession which was held here and at which all the prominent French doctors of America, and his old teacher, Dr. Pozzi, attended.

After that Dr. Harwood was actively associated with the many projects promoting the welfare of the hospital and the university. He was also the moving spirit in the patriotic effort resulting in the foundation of the General Military Hospital of Laval (No. 6), located at Joinville-le-Pont, near Paris, during the Great War.

Dr. Harwood was elected dean of the medical faculty of Laval University in succession to the late Dr. E. P. Lachapelle in August, 1918, and for many years was regarded as the accredited link between the English and French members of the profession.

Besides this he held the following offices. Professor of Gynaecology at the University of Montreal; superintendent of the University Council; president of the Administrative Bureau of the Notre Dame Hospital; president of the Radium Institute; corresponding secretary of the Surgical Society of Paris; vice-president of the Royal College of Medicine in Canada; vice-president of the Association of French-speaking Doctors of North America; a Fellow of the American College of Surgeons, a member of the General Board of Examiners; president of the Medical Union of Canada; vice-president of the Cercle Universitaire; an officer of the Legion of Honour of France.

His chief hobby was farming and cattle breeding. He was vice-president of the Holstein Breeders of Quebec, and his farm, "Het Loo", at Vaudreuil, is noted for its herd of Holstein-Friesian cattle.

He was a director of and a contributor to *L'Union Médicale du Canada* for fifteen years.

He is survived by his widow, formerly Berthe Brosseau; a sister, Mrs. W. K. de Kappelle; two daughters, Mrs. Bernard Languedoc, and Mrs. C. F. C. Porteous; and one son, William Harwood.

### AN APPRECIATION

Of very few men can it be said that he who approaches him, speaks to him, or deals with him, in any way, leaves his company with a higher degree of admiration for his personality and a certain satisfaction of having advanced a step further towards the end he is aiming at. Louis de Lotbinière Harwood was one of these. He always said the thing which best answered the questions asked, and he thus satisfied the hardest to please.

He mixed with everybody: the suppleness of his character allowed him to bend over a cot in a mansard

or over the bed of a public ward in a hospital with a kindness and a piteousness only equalled by his dignity and his delicacy towards his private patients. His knowledge and his ability were equally well employed in the service of both these.

His name belonged to the two ethnical groups which constitute the Canadian nation. In fact, he combined in a rare degree the characters of the French and English people. He was the constant medium of professional relations between the two elements of the country. His name was known throughout Canada and had crossed the seas. He was officer of the Legion of Honour.

His prestige has rarely been equalled. His charm and his distinguished manners had gained for him the respect of every one whom he met. His high stature, the dignity of his bearing, the distinction of his gesture commanded general attention. His social relations were numerous and no important event would have been complete had not the name of de Lotbinière Harwood been inscribed on the list of guests.

His professional probity, his knowledge of medicine, his skill in diagnosis, his operative ability, had placed him at the summit of his specialty amongst the French-Canadians, and as an admiring colleague named him, he was really the "Father of Gynaecology" amongst the French-speaking confrères, having succeeded to Doctor Brennan at a very early age.

All these qualities contributed to his election to the deanship of the Faculty of Medicine of the University of Montreal, sixteen years ago, although he was not the eldest of the professors, by far. He was re-elected every year since then, unanimously, by his colleagues of Council. The Notre Dame Hospital where he served, chose him its President.

He largely contributed to the development of these two institutions that had chosen him to be on their staff. The charitable works he honoured by his patronage used the prestige of his name with advantage; he would encourage them by his words, his writings and his pecuniary aid.

With the death of Harwood, the Notre Dame Hospital loses a capable President, the Faculty of Medicine an esteemed Dean, the medical profession a reputed gynaecologist, the Canadian people, and Quebec in particular, a gentleman, with all the meaning this word implies.

LÉON GÉRIN-LAJOIE, F.R.C.S.(C.)

**Dr. Leeming Carr**, of Hamilton, Ont., sheriff of Wentworth County and former minister without portfolio in the Ferguson cabinet, died suddenly on June 6, 1934.

The scientific, political and administrative ability of Dr. Carr was admitted and he manifested a kindly and cheerful demeanor. He would have attained the age of 70 had he lived until December 21. Dr. Carr was born in Glanford township and acquired his early education in the public schools of Hamilton, after which he went to the University of Toronto (M.B., 1885). He also took degrees at Glasgow and Edinburgh (L.R.C.S.Edin. and L.F.P.S.Glasg., 1886).

**Dr. John Robert Dales**, of Dunbarton, Ont., died on May 5, 1934, in his eightieth year. He retired about six years ago, having practised medicine in Dunbarton since 1885. Dr. Dales was born at Drayton, Ont., and was a graduate of Victoria University (1885). He is survived by his widow, formerly Miss Mary J. Dunbar, and one son, J. Frank Dales, Toronto barrister.

**Dr. A. A. Dechman**, of Bridgetown, N.S., passed away on April 20, 1934, at his home. He had been in poor health for the past two years, and for several months had been confined to his bed. Dr. Dechman was born in Sherbrooke, N.S., in 1862, and graduated from Dalhousie University in 1890. His first practice was in Musquodoboit, from there he moved to the State of Montana, then to Wedgeport, Yarmouth County, from which place he moved to Bridgetown. He had been in practice there for the past twenty-five years.

**Dr. John Irwin Ferguson**, of London, Ont., died on May 10, 1934, in the Toronto General Hospital after an operation performed ten days previously. He was in his 57th year.

Born in London, Ont., the son of Dr. Robert Ferguson, after two years in Arts at the University of Western Ontario, he entered the medical faculty, graduating in 1900. He was for a year an interne at Victoria Hospital, and then a year as house physician at St. Joseph's Hospital. Locating at Courtright, he practised there for several years, returning to London in 1914, in partnership with his father. Since that time he had specialized in diseases of children.

Dr. Ferguson was a member of St. John's Lodge, No. 209, A.F. & A.M., of the London Chapter Rose Croix, London Lodge of Perfection, Moone Consistory of Hamilton, and Mocha Temple of the Shrine. For many years he was on the staff of the University of Western Ontario in the Department of Pædiatrics. He was also a Fellow of the American College of Physicians; a past-president of the Harvey Club of London, and a member of various golf and service organizations.

Surviving are his wife, formerly Miss Josephine Smith, daughter of the late Canon Smith, of London; three sons, Dr. Robert, Jack and Donald, all of London; and a daughter, Mrs. J. R. Wilkey.

**Dr. G. Arthur Ferron** died in New York on April 23rd at the age of 56. He was born at Grand'Mère, where he had been in practice for some 34 years, after graduating from the University of Laval, Montreal (1900).

**Dr. John Ralph Good**, Chaplin, Sask., died at the age of 41 in a Moose Jaw hospital on May 3. Dr. Good was born in Manitoba where he received his education. He graduated from the University of Manitoba, receiving the gold medal from the medical college in 1919. Following his graduation he was house surgeon at the Winnipeg General Hospital for a period of two years, after which he took up his practice at Tuxford, Sask. He also practised at Oak Lake, Man., Battleford, Sask., and Chaplin, Sask. Dr. Good always considered the welfare of the patient first, and lack of finances did not hinder the administration of the necessary treatment. He was good at athletics, especially hockey and baseball. He is survived by his mother, of Virden, Man.; one sister, Mrs. C. Houston, of Winnipeg; and a brother, Dr. H. S. Good, of Weyburn, Sask.

**Dr. Andrew Grant**, of Beaverton, Ont., who had practised in Beaverton and the district for forty-eight years, died on May 23, 1934, in his eighty-first year. He was born near Lorneville in 1853 and was a graduate of the University of Toronto (1877). He is survived by his widow, formerly Miss Mary Jane Watson; three daughters, Mrs. E. A. Holmes and Mrs. J. W. Fowler, Toronto; Miss Elsie Grant at home; one son, James George Grant, Toronto, and two grandchildren.

**Dr. John Francis Hart**, of Athens, Ont., who had practised there since 1888, died on May 4, 1934, following a surgical operation. He was a native of Osnaburck, Ont., and a graduate of Queen's University (1887). He had served as coroner for Leeds and Grenville.

**Dr. Philip Reide Kaiser**, of Tottenham, Ont., died at his late residence, on June 3, 1934, in his 33rd year. He was a graduate of Queen's University (1926), and a Licentiate of the Medical Council of Canada.

**Dr. Gordon Russell MacKay**, of Hagersville, Ont., was killed, and his wife injured, on June 4, 1934, when the auto he was driving apparently got out of control and after running for a distance along the shoulder of the road swerved into the ditch and rolled over pinning the doctor under the machine.

Dr. MacKay was the son-in-law of R. S. Solter, K.C., of Cayuga, and was thirty-one years of age. He was a graduate of the University of Western Ontario (1927).

**Dr. Murdoch Angus MacKay**, of Tisdale, Sask., died at Victoria, B.C., on April 1, at the age of 54 years. He was born at Baddeck, N.S. He taught school in the West in 1901 and graduated from Queen's University in 1911. He spent a few months in practice with Dr. J. V. Connell, then went to Indian Head. Later in the Fall of 1911 he settled in Tisdale.

Last year Dr. MacKay was elected to Grand Master of Saskatchewan, the highest office to which a Mason can be elected. In politics he was a strong Conservative and was president of the Conservative Association for the Federal Constituency of Melfort at the time of his death. For over eighteen years he was a member of the Tisdale school board, most of which time he was chairman. He was an elder in St. Andrew's Presbyterian Church.

For the services rendered by him to the war veterans, their wives and families, he was made an honorary member of the Tisdale branch of the Canadian Legion. Throughout the years of war he treated a large number of soldiers' families and his remuneration was the pleasure he got from such actions. Since the war he fought hard for the betterment of the conditions of the returned men and aided in the securing of pensions for the needy ones.

Dr. MacKay had an excellent sense of humour, was a clever conversationalist, and could tell many good stories of pioneer days. He had a good library and kept up in his work, had a snowmobile, and made lots of hard trips in winter. He was the kindest thing in the world, but as firm as iron and determined.

He is survived by his widow, the former Elena Lindeburg, one daughter, Margaret Catherine, and one son, Malcolm Ian; also by two brothers, Angus and Malcolm, and four sisters who live in Nova Scotia.

A pleasing incident occurred when, departing from the usual Arbor Day program, the students of the Tisdale public and high schools planted an elm tree in memory of the late Dr. M. A. McKay. The ceremony was very effective. About three hundred and fifty boys and girls formed three rings around the centre of the lawn where the tree was planted, while a large number of citizens also gathered. Accompanied by the Tisdale band, the students opened the ceremony with "The Maple Leaf Forever." Mr. L. T. Carmichael, principal of the schools, acted as chairman and also gave an address on the value of trees to the community. The tree was planted on behalf of the school board by the Chairman, Mr. R. C. Farr assisted by Mr. George McMurdo.

T. H. P. Lamb, mayor of Tisdale, following the planting, delivered the dedication speech. Stressing the years of unselfish and devoted service in which Dr. McKay had spent in furthering educational advances in this community, the speaker committed the



tree to the care and continued protection of all the boys and girls of the district. Mrs. A. Bernz then sang Joyce Kilmer's poem, "Trees."

At a regular meeting of the town council the question of dedicating the eighteen acre park site recently donated to the town by the Saskatchewan Power Commission was brought up for discussion, and it was unanimously agreed that this should be named "McKay Park," in memory of Dr. McKay, who had devoted over twenty-two years of his life to the medical care of the residents of the district and in many other ways contributed much to the welfare of the community.

LILLIAN A. CHASE

**Dr. Arthur David Morgan** died at his home in Port Alberni, B.C., recently. The late Dr. Morgan, who graduated from McGill in 1901, had practised in British Columbia for more than thirty years. During the war he served overseas with the C.A.M.C. He is survived by his widow.

**Dr. Frederick William Mulligan**, of Petrolia, Ont., died on May 11, 1934, from pneumonia. He was born at Millbrook, Ont., and a graduate of Trinity Medical School (1893). He held the L.R.C.S.(Edin.), 1894; and the L.R.C.P.(Lond.), and M.R.C.S.(Eng.), 1895. He was 62 years old and had practised in Petrolia for thirty-eight years. Dr. Mulligan was a former member of the Petrolia Board of Education, and was prominent in lodge and community affairs. He also was coroner for Lambton County. Dr. Mulligan was a radiologist and head of the x-ray department of the local hospital. He is survived by his widow, formerly Miss Franc de la Matter, of Owen Sound; three daughters; and two sisters, Mrs. Aiken and Miss Mulligan, of Port Hope; and one brother, Arthur Mulligan, of Cleveland.

**Dr. John Edward Reeve**, of Toronto, died at his residence on May 10, 1934.

**Dr. R. Hunter Robinson**, one of Toronto's oldest practitioners, died recently in the Toronto Western Hospital at the age of 87.

Oldest house surgeon at the Toronto General Hospital, Dr. Robinson had devoted his time in recent years to assisting mental patients.

It had been his proud boast that during 53 years of active practice he never lost a woman patient.

Dr. Robinson believed music had a soothing effect upon certain types of sufferers, and a woman singer usually accompanied him on his hospital visits. He had a good voice himself and recently sang a solo in public. He was regarded as an authority on the Bible, and rather than take personal credit for his success in medicine, had always maintained he applied "faith with works."

A native of Bond Head, Dr. Robinson graduated from the old Toronto Medical College about 1870. His son, Justin Robinson, survives.

**Dr. James George Ross**, of Embro, Ont., and formerly a resident of London, died on May 13, 1934 aged 67 years.

James George Ross was the last surviving son of the late Mr. and Mrs. J. M. Ross, of Embro. In 1897 he was the operator of a drug store on Richmond Street and was widely known in London. He graduated in medicine from Chicago Medical School and practised there for ten years prior to going to Alberta, where he operated a farm and continued his practise

of his profession. Two years ago when his health failed he returned to Embro.

Surviving beside his widow, are two sisters, Mrs. John Stewart, of North Dakota; and Mrs. A. T. Bell, of Tavistock, Ont. Brig. Gen. J. M. Ross, G.O.C., M.D. No. 1, London, and Lieut-Col. R. B. Ross, London, are nephews.

**Dr. William Spankie**, of Wolfe Island, Ont., Conservative member in the House of Commons for Frontenac-Addington, died in the Kingston General Hospital, on May 27, 1934. He was 74 years of age and had been ill for some time.

Dr. Spankie was born in Kingston, October 17, 1859, the son of William Creig Spankie and Margaret Ann Lanktre. He was educated in Kingston private and public school, the Kingston Collegiate Institute and Queen's University, obtaining his degree of bachelor of arts in 1882 and the medical degree in 1885. He settled at Wolfe Island after he graduated and he later was selected public school inspector for the county, a position he held for twenty-six years. In 1912 he was elected reeve of Wolfe Island and the next year was chosen warden of the County of Frontenac.

For sixteen consecutive years he represented his township in the county council of Frontenac, retiring from municipal politics to accept the Conservative nomination after the death of Hon. Dr. J. W. Edwards in 1929. He was successful in the by-election and the next year at the general elections he defeated Samuel Stinchcombe, Liberal, by a 3,371 majority.

Dr. Spankie had been coroner for Frontenac since 1901 and was one of the most learned of medical graduates of Queen's University. He had been a member of the Medical Council of Ontario since 1901, and a Past-president of both the Ontario and Dominion Medical Councils. He had one daughter, Mrs. A. S. Kennedy; and four sons, Dr. W. E. Spankie, Dr. A. T. Spankie, R. M. Spankie, of Calgary, and H. L. Spankie, of High River, Alta. Mrs. Spankie also survives.

Dr. Spankie was one of the last of the old-time country doctors. While on Wolfe Island for 45 years he attended families to the third generation. His practice extended over an island twenty-two miles long.

**Dr. Armstrong M. Spence**, of Lucknow, Ont., died in Oshawa Hospital, on June 2, 1934. Dr. Spence was a graduate of Trinity Medical College (1889). He is survived by his widow; two sons, Dr. R. Armstrong Spence, of Amsterdam, N.Y.; and James L. Spence, B.Sc., of Montreal; and two daughters, Mrs. William Karn, of Oshawa, and Mrs. A. A. Cameron, of Ottawa.

**Dr. Thomas John Clayton Tindle**, of Flinton, Ont., died on May 21, 1934, in Belleville General Hospital, after an illness of a month. The late Dr. Tindle had practised in Flinton for thirty-one years, coming to that community from Peterborough directly following his graduation from Trinity University (1903). Fifty-eight years of age, he was known throughout Hastings and Lennox and adjoining counties. He was a staunch Conservative in politics, and was a strong supporter of the temperance cause. The late Dr. Tindle is survived by his widow and half-sister, Miss May Jorie, of Peterborough.

**Dr. Eugene Walters**, aged 69, died in Winnipeg on May 9th after a long illness. Born in London, Eng., he was educated as a missionary and in 1887 went to a mission field in Jamaica. He graduated in medicine in 1896 from the University of Minnesota, and in 1903 came to Winnipeg, where he established a clinic in North Winnipeg, and later served on the staff of Victoria Hospital.



## News Items

### Alberta

Following the action of the Legislature of Alberta, when it adopted the basis of health insurance in the report of the special Commission, the Provincial Department of Health is preparing to organize a special Health Unit, in which to test out the scheme. They are choosing a district with a good municipal hospital, surrounded by a good farming district, where crop failures seldom if ever occur. The department is asking the College of Physicians and Surgeons for a set of fees, based on all work paid for, and the matter is receiving serious attention. If the area planned for votes in favour of the financial obligation involved, it is expected that enabling legislation will be passed next winter. The Government will have to include a financial grant, equal to two-ninths of the cost of the experiment, in its next budget.

At a recent meeting of a municipal council, the question of assuming the financial obligations for the medical care and treatment of indigent sick residents was up for discussion. One councillor suggested that the profession should have a fixed fee for appendicectomy and in a similar manner for all other common operations. The representative of the profession, who was present suggested that following such an arrangement, the farmers agree to fix definite prices for the things they sell. As a horse was a horse and a cow was a cow, so all horses should sell at the same price. The farmer councillors saw the point and the matter was dropped.

The Council of the College of Physicians and Surgeons of Alberta, while not recognizing as ethical all contract practice, has sent out a plebiscite to the profession, to ascertain if it is the wish of the members that the Council be a clearing-house for all suggested contracts. In the replies it has been found that owing to the depression, municipal councils have been making very hard bargains with some members of the profession. In one case a physician cares for the health duties of the community as well as for the indigent sick on a basis of 15c. a mile for every mile travelled! It seems most unreasonable that a physician should be expected to be out of pocket in rendering a service which is the obligation of the whole municipality.

Notwithstanding the fact that all graduates in medicines of the University of Alberta are entitled to registration in Alberta, without further examination, twenty-one out of twenty-four graduates have been issued enabling certificates, to try the examinations of the Medical Council of Canada.

The College of Physicians and Surgeons of Alberta annually makes grants for five scholarships to medical students in the University of Alberta. This year each of the following students won a scholarship: final year medicine, John Smith Gardner; final year surgery, Clarence Edward Holmes; third and fourth year physiology, James Francis Elliott; second and third year anatomy, John Melling; second year proficiency, Ralph Mayo.

G. E. LEARMONTH

### British Columbia

On May 13th, the newly-completed Crippled Children's Hospital of Vancouver was opened by the Acting-Premier. It was stated that it has taken those responsible fifteen years to accumulate the funds necessary for this enterprise.

It is announced that a psychiatric clinic will be opened in Victoria in the near future. The administration will be under the Provincial Mental Hospitals.

A study of the vital statistics for British Columbia for the month of April shows that during that month there were 49 deaths from cancer, 37 from tuberculosis, and only 2 from puerperal sepsis.

Since 1930 the fire department of Vancouver has been equipped with a number of inhalators for use in asphyxia. Figures recently published show that since then, these devices, in the hands of specially trained crews, have resuscitated 78 cases of asphyxia from noxious gases and 23 cases of drowning.

C. H. BASTIN

### New Brunswick

Dr. Robert A. H. MacKeen has been appointed Director of the Bureau of Laboratories for the Province of New Brunswick, succeeding the late Dr. H. L. Abramson. Dr. MacKeen took up his new duties on June 1st. For the last five years he has been Assistant Professor of Pathology at Dalhousie University, Halifax, and Assistant Pathologist for Nova Scotia. Dr. MacKeen is a Maritimer-born, coming from Cape Breton.

The Provincial Government announced on May 16th, the appointment of Dr. Ray Landry, of Moncton, to the Council of the College of Physicians and Surgeons of the Province of New Brunswick, to succeed the late Dr. Murray.

Graduations from the various nursing schools of the Province are being announced in the press daily. At many of these graduations, doctors of prominence are the chief speakers. At the Hôtel-Dieu, Chatham, Dr. Herbert Morrissey presented the prizes. At the graduation for the Moncton City Hospital, Dr. W. A. Ferguson addressed the class of 13 graduates on May 12th, while Dr. Wm. F. Roberts, chief of the Department of Physical Therapy at the Saint John General Hospital, was the speaker to the graduating class of 21 nurses from the Saint John General Hospital on June 7th.

At the final meeting of the Saint John Medical Society in May, Dr. J. R. Nugent, of the surgical staff of the General Hospital, was the speaker. Dr. Nugent presented a summary of the operative cases of appendicitis in the two Saint John hospitals for a period of three years. He discussed the type of disease present clinically as compared with the type of disease found at operation. He analyzed the results of the series, and it was found that the mortality rate per hundred thousand population and the mortality percentage of cases operated on compared extremely favourably with any other recorded figures. Dr. Nugent laid stress on the fact that early diagnosis in this community was the rule, and that, even including cases from the county which were rural rather than suburban, the results indicated a high degree of cooperation between referring physicians and surgical staff. This paper was extremely interesting to the large gathering which heard the discussion, and perhaps of the papers presented during the past winter the palm for excellence should be awarded to Dr. Nugent's effort. This final meeting was a satisfactory conclusion to the successful series of meetings addressed by local men since the discontinuance of the Canadian medical extra-mural courses. The local executive have been highly congratulated on the success of these meetings.

The Executive of the New Brunswick Medical Society met in Woodstock on May 18th, to complete arrangements for the meeting of the New Brunswick

Medical Society, to be held in Woodstock on July 10th and 11th. An excellent program has been arranged. Local arrangements are in the hands of Dr. J. F. L. Brown. An invitation has been extended to the medical men of Aroostock County, Maine, to attend this meeting across the border in New Brunswick.

Dr. L. DeV. Chipman, Chief of the Nose and Throat Department of the Saint John General Hospital, Saint John, has just returned from Great Britain, where he undertook some further post-graduate studies.

Dr. Geo. F. Skinner, of the surgical staff, is continuing his studies in Great Britain at present.

Drs. J. M. Barry, A. E. Macaulay, Mayes Case, and W. J. Baxter have just returned from Halifax, having completed their duties as examiners for the Dominion Medical Council.

A. STANLEY KIRKLAND

### Nova Scotia

A meeting of the Nova Scotia Society of Mental Hygiene recently held at the School for the Blind had as special speaker, G. M. Hatfield. The subject of his lecture was "Physiotherapy in the treatment of mental and nervous ailments". This lecture is one of a series on "Modern methods in mental hospitals" sponsored by the Society with a view to bettering facilities in mental institutions in the province.

The Nova Scotia Medical Society will hold its annual meeting at Yarmouth on July 4th and 5th next. All indications point to a large attendance. Several prominent visitors will deliver papers. Dr. G. W. Crile, of Cleveland, and Drs. E. P. Joslin, Frank H. Lahey, Gilbert Horrax, and H. M. Clute, of Boston, will attend, in addition to representatives from the Provinces of New Brunswick and Prince Edward Island. The social program has been drawn up with as much care as the medical. Patrons at the banquet and dance will be Lieutenant-Governor W. H. Covert and Mrs. Covert, Premier Angus L. Macdonald and Mrs. Macdonald, and the Honourable F. R. Davis and Mrs. Davis.

Dr. R. A. H. MacKeen, for the past five years Assistant Professor of Bacteriology and Pathology at Dalhousie University, has resigned from the staff of the university to undertake his new duties as Pathologist for the Province of New Brunswick in succession to Dr. Abramson. Before leaving, Dr. MacKeen was guest of honour at a banquet given by a group of his associates.

Three new appointments to the staff of the Victoria General Hospital, Halifax, were made recently. They are: Dr. R. A. Noble, a graduate of Acadia and Edinburgh Universities; and Drs. Edwin Ross and Arthur Murphy, graduates of Dalhousie University, who are appointed Assistant Attending Surgeons; Dr. G. A. Winfield has been appointed Assistant in Urology at the Public Health Clinic of Dalhousie University. Also, it may be noted, a full urological service has been established at the Victoria General Hospital, under Dr. Frank G. Mack.

Dr. H. G. Grant and Dr. A. MacLean, of the Department of Hygiene of Dalhousie University, attended the meeting of the Canadian Public Health Association held in Montreal in June.

The 27th Annual Meeting of the Valley Medical Society was held in Middleton on the 22nd ultimo. Dr. R. L. Braine presided. The guest-speaker was Dr. E. K. McLellan, of Halifax, who took as his subject "Obstetrics". Dr. P. S. Cochrane, of Wolfville, was elected *President* for the following year.

N. B. DREYER

### Ontario

Dr. J. P. Morton, of Hamilton, has been named chairman of the Medical Board of the Hamilton General Hospital.

We learn from a recent announcement of the Honourable Dr. Robb, Minister of Health for Ontario, that the Province now has a total supply of 2,100 milligrams of radium, which is being used in the Cancer Treatment Centres.

Realizing the great advance made in the treatment of pulmonary and other forms of tuberculosis through various forms of surgical therapy, the Queen Alexandra Sanatorium is contemplating the addition of a new surgical pavilion.

The Health Department of the City of Hamilton, in its decision to decentralize the health clinic for the benefit of the public, opened, in the month of May, a branch clinic of the Department of Health as an eastern centre. For the present 12 nurses, 2 dentists, a dental assistant, and a clerk will be on the staff.

Dr. R. J. P. McCullough, of Toronto, returned about June 1st from a visit to China. Most of his time was spent in medical mission centres in special ophthalmological work. He worked from early morning until late at night, assisting the mission doctors in their work among the Chinese. Trachoma is reported to be one of the most frequent complaints.

The staff of the Department of Medicine of the University of Toronto tendered to their chief, Professor Duncan Graham, a complimentary dinner at the University Club, on May 29th, in honour of his election as a Fellow of the Royal College of Physicians of London. Some sixty or more were present.

Dr. Ward Woolner, of Ayr, has recently been elected President of the Canadian Health Officers' Association.

The Alumni Association of the University of Western Ontario Medical School has elected for next year, the following officers: *President*, Dr. J. A. Macgregor; *Vice-presidents*, Drs. E. L. Williams and Geo. A. Ramsay; *Treasurer*, Dr. Fred Luney; *Secretary*, Dr. J. W. Crane.

Under the direction of the Northern Ontario Relief Commission, a dental coach is leaving shortly to operate in Northern Ontario as far west as the Manitoba boundary, assisting settlers in free dental treatment. Formerly, under the Commission, the equipment operated by railway coach, but, with a view to reaching all sections of the country, a new motor coach was built and equipped under the direction of W. H. Alderson, Chairman of the Commission. Dr. B. L. Washburn is in charge.

J. H. ELLIOTT

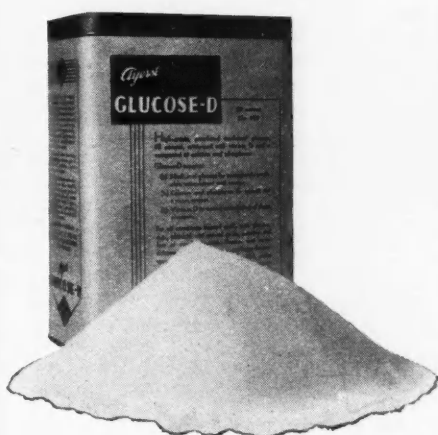
### Quebec

Dr. Colin K. Russel, of Montreal, was elected President of the American Neurological Association at its 60th annual convention at Atlantic City, N.J., on June 6th.

He succeeds Dr. Israel Strauss, of New York.

Dr. Russel is clinical professor of the department of neurology and neurosurgery at McGill University.

Dr. E. W. Archibald, of Montreal, Chief Surgeon to the Royal Victoria Hospital and Professor and Director of Surgery, McGill University, was elected President of the American Surgical Association at the annual convention at Toronto, on June 7th. The delegates concluded the meetings recently.



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Other officers are: *Vice-presidents*, Dr. David Cheever, Boston and Dr. Mont Reid, Cincinnati; *Secretary*, Dr. Vernon C. David, Toronto; *Treasurer*, Dr. B. Fordyce, Saint John, N.B.; *Recorder*, Dr. Walter E. Lee.

The thirty-fourth annual meeting of the Canadian Tuberculosis Association was held in Montreal from June 11th to 13th, with a most satisfactory attendance and an extremely interesting and instructive program. The first day was devoted to the reading of papers. On the following day there was a clinical session at the Royal Victoria Hospital at which a brilliant address was given by Dr. E. W. Archibald on "Relative indications for thoracoplasty and phrenicectomy." The members then adjourned for luncheon at the Sacred Heart Hospital, Cartierville, where clinical demonstrations were given by members of the staff. The final clinical session was given at the Royal Edward Institute on the next morning when selected cases at the Institute brought out most interesting and valuable discussion.

This meeting was held in conjunction with the Canadian Public Health Association and it will be long remembered as one of the most stimulating and lively conventions held in this city.

### United States

**The Society of American Bacteriologists.**—Dr. Milton J. Rosenau, Boston, was elected *President* of the Society of American Bacteriologists at the annual session in Philadelphia on December 28, 1933. Karl F. Meyer, Ph.D., San Francisco, was named *Vice-president*, and James M. Sherman, Ph.D., Ithaca, N.Y., re-elected *Secretary*. Dr. Ludvig Hektoen, retired head of the department of pathology, Division of Biological Sciences, University of Chicago, was elected an honorary member, said to be the first so chosen since 1917.

**The American Congress of Physical Therapy.**—The thirteenth annual scientific and clinical session of the American Congress of Physical Therapy will be held in Philadelphia at the Bellevue Stratford, September 10, 11, 12, 13, 1934.

This year's session will be especially noteworthy because of the excellent program which has been arranged. Outstanding clinicians and teachers will present the results of the newer researches in the field emphasizing short-wave therapy, hyperpyrexia, light-therapy, remedial exercise, massage, and other interesting subjects. On Wednesday evening, September 12th, a joint session will be held with the Philadelphia County Medical Society. Special features will be the scientific and technical exhibits and the small group conferences. The latter have been arranged for Tuesday morning. Every specialty of medicine and surgery will be represented. The technical application of physical measures will be demonstrated and the fundamentals emphasized. The general sessions will be taken up with symposia on cancer, arthritis, poliomyelitis, industrial surgery, etc. Friday, September 14th, has been set aside for hospital teaching; clinics will be held in the leading institutions of Philadelphia.

Physicians and their technicians, properly vouched for, are eligible to attend.

Send for the preliminary program to the American Congress of Physical Therapy, 30 North Michigan Avenue, Chicago, Ill.

### General

**Leprosy in Canada.**—A reduction of \$12,000 in the Dominion Government appropriation for the administration of the Act respecting leprosy led to a question whether there has been any reduction in the number of those so afflicted. In reply the Minister of National

Health stated that at the present time there are fifteen cases of leprosy in the two lazarettos, one at Tracadie, in Gloucester County, and the other at William Head, in British Columbia. The cases at the William Head lazaretto are confined to Chinese, there being five of them. Of the ten at Tracadie only four are Acadian.

Hon. Dr. MacLaren went on to say that the history of leprosy goes back about ninety years in that area of the country. He could recall visiting Tracadie lazaretto about thirty years ago, at which time there were between twenty and thirty cases, all from the surrounding district. To-day out of a total of ten there are only four cases which have come from the sea-coast area, or are connected with Northumberland and Gloucester. The last case from the surrounding country was in the year 1919. In other words, no new case of leprosy has been brought to the attention of the authorities for fifteen years. That is a cheerful fact, and we may look forward with confidence to the disappearance, within a reasonable number of years, of the affliction.

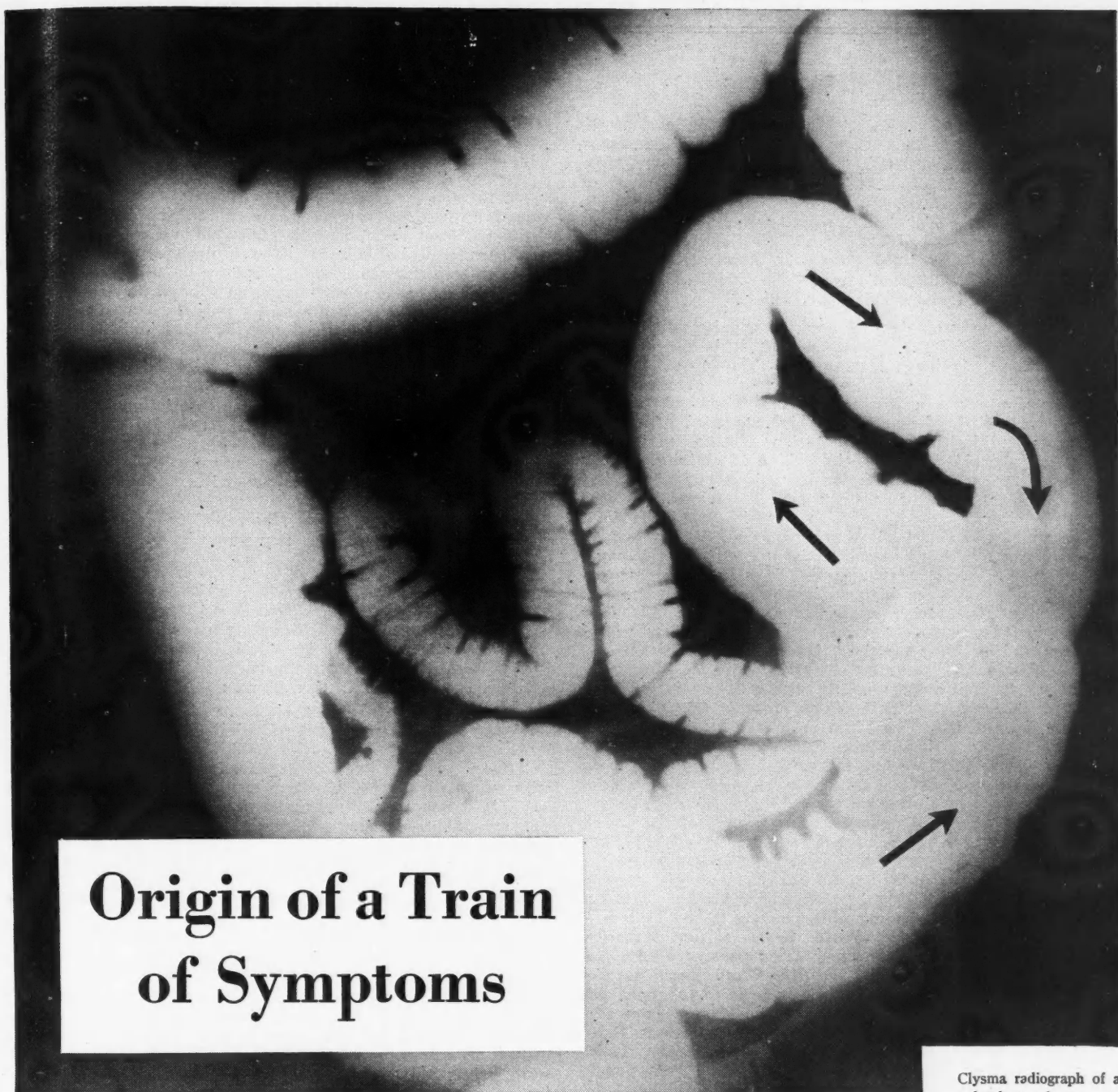
**The American College of Physicians** will hold its Nineteenth Annual Clinical Session in Philadelphia, April 29 to May 3, 1935.

Announcement of these dates is made particularly with a view not only of apprising physicians generally of the meeting but also to prevent conflicting dates with other societies that are now arranging their 1935 meetings.

Dr. Jonathan C. Meakins, of Montreal, is President of the American College of Physicians, and will arrange the Program of General Sessions. Dr. Alfred Stengel, Vice-president in Charge of Medical Affairs of the University of Pennsylvania, has been appointed General Chairman of local arrangements, and will be in charge of the Program of Clinics. Mr. E. R. Loveland, Executive Secretary, 133-135 S. 36th Street, Philadelphia, Pa., is in charge of general and business arrangements, and may be addressed concerning any feature of the forthcoming Session.

**The Royal College of Physicians.**—We are pleased to announce that Dr. Duncan Graham, Chief of the Department of Medicine, Toronto University, has been elected to Honorary Fellowship in the Royal College of Physicians of London.

**Canadian Society for the Study of Diseases of Children.**—The twelfth annual meeting of this Society was held in Brockville, Ont., June 1st and 2nd, with a good attendance of over fifty. A series of extremely interesting papers was given, of which Dr. L. J. Austin's address on "Medicine of the eighteenth century," was perhaps the most interesting in a general way. The paper by Dr. Cushing on "Addison's disease in childhood," was a striking contribution and provoked a great deal of discussion. Dr. Alan Ross presented a paper on "Von Gierk's glycogenetic hepatomegaly with report of a case" which was also worthy of note. A paper by Drs. Drake, Tisdall and Brown on "Clinical comparison of value of various antirachitic substances" showed that in a large group of infants in Toronto one teaspoonful of cod liver oil was as effective as three in the prevention of rickets and that rickets was a particularly universal disease in the absence of specific preventive treatment. The paper by Elizabeth Chant Robertson tended to show that the laxative value of certain foods was due to their high potassium content. The paper by Dr. A. P. Hart, Toronto, discussing the "Problem parent" suggested that common sense rather than psychology was necessary for the treatment of the problem child.



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## Book Reviews

**The Journal of Technical Methods and Bulletin of the International Association of Medical Museums, No. XIII.** Edited by Maude E. Abbott, M.D., Montreal, Canada, with the collaboration of William Boyd, M.D., Winnipeg, Man., Carl V. Weller, M.D., Ann Arbor, Mich., and Robert A. Moore, M.D., New York, N.Y., Editorial Board. March, 1934, 204 pages, 33 illustrations. Price \$2.00. Published from The Medical Museum, McGill University, Montreal.

This valuable journal occupies a quite unique place among medical periodicals, in that it is the only one functioning in its particular field. The present number, which is a large well-illustrated volume of nearly 300 pages, presents a distinct advance upon all previous issues, both in the uniformly high standard of its contents and in the strict limitation of these to what is rightly considered its special sphere of activity, namely contributions, abstracts and reviews on Technical Methods, Cardiac Anomalies and Teratology, and the Proceedings of the Association of which it is the official organ. A leading editorial informs us that this is in accordance with a new policy inaugurated by its management, which has undertaken also to make this an *annual* instead of an *occasional* publication. Editorial acknowledgment is further made of a grant of \$5,000.00 received by the Association from the Carnegie Corporation of New York for the upkeep of its publications.

The volume contains, in addition to book reviews, abstracts and reports of the Proceedings, 32 original contributions, of which 5 are on Museum Administration and Equipment, 13 on Museum and Autopsy Technique, 1 on Photographic Methods, 7 on Microscopic Technique, and 5 on Cardiac Anomalies. The introductory one among these is a richly illustrated descriptive article on the Museum of Pathology of the University of Toronto by J. L. Little. Other outstanding contributions are a highly spectacular communication by Pedro Ara, of Madrid, Spain, on "A New Process of Embalming" by a method of paraffinization; "An Attractive Cell for Thin Cross-Sections" by James Davies, of Detroit; "Suggestions for Sealing Museum Jars in the Tropics" by Juliana Smetana, Porto Rico; "New Autopsy Table" by H. C. Schmeisser, Tennessee; "Technique for the Demonstration of the Specialized Tissue in the Heart," by Helen Taussig, Baltimore; "Aneurysm of the Interventricular Septum," by Eric Massig, Toronto; "Congenital Aortic Atresia," and "Anomalous Subclavian Artery" by Vera Dolgopol, New York. It is closed by two important reports under the International Index descriptive of the Pathological Museums of *Austria* and *Italy* by Prof. R. Maresch, of Vienna, and Prof. Binde de Vecchi, of Florence, and a Report of the Meetings of the British Local Section by its Secretary Dr. Sydney Daukes, Director of the Wellcome Museum of Medical Science, London. A list of the membership to date appended shows 248 enrolled in its American and Canadian group, 19 in the British, and 48 in Foreign Local Sections.

As in the preceding numbers of this journal, this very representative volume has been put out by the Murray Printing Company, of Toronto. In its general makeup and illustrations it ranks with the best class of medical periodicals.

**A Sixth Venereal Disease.** Hugh Stannus Stannus, M.D., Ph.D., F.R.C.P., M.R.C.S., D.T.M.&H., Physician to the French Hospital, London. 270 pages. Price \$3.75. Baillière, Tindall & Cox, London; Macmillan Co., Toronto, 1933.

The title of this book implies that the author considers that a whole group of pathological lesions named, described and recognized in the past as separate entities are in reality due to the same cause. They are, in fact, one disease, a disease he calls "a sixth venereal disease".

The titles of the 21 chapters and 2 appendices reveal a comprehensive approach to the subject. The history of the various aspects of the condition is well treated. There is always something convincing about a historical review, and, when it is well done, it not only adds completeness to a subject but it gives one an insight into the development of our knowledge of it.

The etiology of the Sixth Venereal Disease is reviewed through its various stages, up to and including the more recent work in which a filterable virus has been demonstrated to be its cause. The results of experiments on animals are given. The pathology of the primary and secondary lesion is reviewed in detail and illustrated. One would like to see more and better illustrations of the primary lesions and the lesions in the lymph nodes.

The greater part of the book is devoted to the late manifestations of the disease, a considerable part of which is devoted to Inflammatory Strictures of the Rectum. After reading the discussions on inflammatory strictures of the rectum, such a lesion should at once suggest the Sixth Venereal Disease and call for a properly prepared and properly interpreted intracutaneous reaction of Frei. A chapter is devoted to the consideration of this reaction.

Any one who is passively interested in the subject should read this book, and any one who is seriously interested should study it.

**Principles of Gynecology.** William Blair-Bell, B.S., M.D., F.R.C.S., F.C.O.G., Hon.F.A.C.S., Hon.L.L.D., Gynecological Surgeon, Royal Infirmary, Liverpool. Fourth edition revised by M. M. Datnow and A. C. H. Bell. 848 pages, illustrated. Price \$12.55. Baillière, Tindall & Cox, London; Macmillan Co., Toronto, 1934.

The general arrangement of this book, as found in former editions, has not been altered, but improvements have been made in every chapter and more than 100 illustrations have been added. Since the publication of the 3rd edition scientific advances in subjects such as endometriosis, the pathology and treatment of malignant disease, and endocrinology have been so great that these chapters have been entirely rewritten. The history of gynecology and its advances from the days of Hippocrates to the time of Lawson Tait introduces the volume. Other new chapters on sociological and medicolegal questions have been added. The twelfth section deals with operative technique; various operations on pelvic tumours, inflammatory conditions, repair of birth-injuries, etc., are briefly discussed. Post-operative complications and their treatment, lipiodol injections of tubes, and indications and methods of transfusion are all dealt with at some length. An appendix of classified causes of certain gynecological symptoms is added, to give to the student in synopsized form assistance in making a diagnosis by exclusion, and to serve as a review of the main gynecological symptoms. The writing is clear and attractive, and the general "get-up" of the book is unusually good.

**Handbook of Therapeutics.** David Campbell, M.C., M.A., B.Sc., M.D., F.R.F.P.S., Regius Prof. of Materia Medica and Therapeutics, University of Aberdeen. Second edition, 444 pages. Price \$4.15. E. & S. Livingstone, Edinburgh; Macmillan Co., Toronto, 1934.

This little book opens with short chapters on the management of the sick room and the usual nursing care required, on prescription writing, the methods of administering remedies, diet, physiotherapy and the use of biological products. Following these introductory chapters the treatment of local and constitutional disease is discussed in detail.

For the student and practitioner the book will prove a valuable aid. The directions are clear and reliable, and, although conservative in character, do not neglect the newer methods. The author rightly condemns the necessity of too constantly prescribing proprietary remedies and experimenting with remedies of unknown





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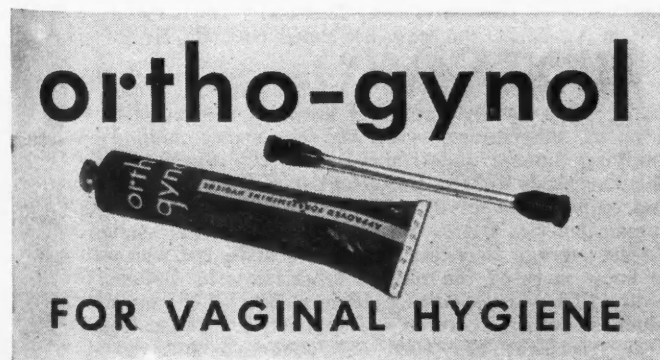
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qualities. He strongly recommends the art of using drugs of known value and of becoming familiar with their action. He supports this view by quoting Whitla's statement, that "The man who is patron of all drugs will too often be found not to be master of a single remedy". We can cordially recommend this work as a concise and reliable guide in medical treatment.

**The Common Diseases of the Skin.** R. Cranston Low, M.D., F.R.C.P., Consulting Physician to Skin Department, Royal Infirmary, Edinburgh. Second edition, 317 pages, illustrated. Price 12/6 net. Oliver & Boyd, Edinburgh, 1934.

Practical usefulness is the key-note of this small book. It has been designed for the special needs of the general practitioner, and within its compass it contains a large amount of useful information about the recognition and the nature and treatment of the commoner skin diseases. The reader is spared the distraction of foot-notes and bibliographical references and is not overwhelmed with a mass of theory and variety of methods of treatment, which so frequently serve only to confuse. The introductory notes on anatomy, physiology, symptomatology and treatment are concise and lucid. A few inaccuracies, such as the statement (p. 10), "scabies itches only at night", are probably the result of striving for brevity. The writer's style is easy and pleasant throughout.

Although reference to syphilis is frequently made in the discussion of differential diagnoses, no space whatever is given to syphilis itself. In view of the general recognition of the inseparability of dermatology and syphilology, that an understanding of syphilis demands a thorough acquaintance with dermatology, and that the study of dermatology must include the study of syphilis, it is felt that a serious omission exists in this respect.

The illustrations are numerous. The photographs, including 8 colour-plates from moulages, are of average quality; a few are exceptionally good. Two very commendable features are the diagrammatic drawings illustrating the histopathology of various skin lesions, and the rough pen-and-ink sketches depicting the characteristic distribution of certain dermatoses.

As a handbook for the student and the man in general practice this volume will furnish an answer to many of their dermatological difficulties, and should be generally welcomed.

#### **Intercortical Systems of the Human Cerebrum.**

Joshua Rosett, Assistant Professor of Neurology, Columbia University. 135 pages, illustrated. Price \$3.00. Columbia University Press, New York, 1933.

As the title indicates this is a monograph dealing with the intricate problem of the subcortical and intercortical fibre-connections of the human cerebral cortex. The approach to this study has been made with the aid of a new and ingenious technique for the display of these short and complicated pathways. A description of the technique for the complete preparation of specimens for study is given in detail in the second chapter. To the novice the technique appears rather difficult and tedious, but in the hands of the author it has yielded further convincing information regarding these tracts and, incidentally, cerebral fissuration. The sixth to the thirteenth chapters, inclusive, contain in turn brief accounts of the intercortical systems as found with the author's technique in the various areas of the cortex, and many findings are of interest. Chapters three, four and five, introductory in character, are very brief, discussing questions in respect to the limitations of the technique and the author's views regarding the cell origin of the intercortical systems in general, and an explanation concerning annectant convolutions. The author felt it premature in the present work, however, to attempt a correlation of "the course and direction of any of the numerous intercortical pathways mapped out with any of the cortical cell areas delineated by

cause of fissuration built on the new observations of the present work, which, in the light of the authoritative literature there reviewed, is very plausible.

This has been a painstaking work and the author deserves credit. The text is, for the most part, clearly written. The volume is not a textbook, and is of interest and of practical importance to those particularly interested in this special part of neuroanatomy and of neurophysiology. It should broaden the viewpoint of those interested in neurology, epilepsy and psychology.

**Chances of Morbid Inheritance.** Edited by C. P. Blacker, M.C., M.A., M.D., M.R.C.P., General Secretary of Eugenics Society. 449 pages. Price 15s. net. H. K. Lewis, London, 1934.

This book aims to give the physician a basis for understanding the laws of heredity, and for dealing with the questions of his patients as to the chance of transmitting defects to their offspring. The section dealing with hereditary diseases of the nervous system is excellent, as is the section on the theoretical considerations of inheritance. The chapters on mental disease, mental any of the investigators of that subject." The final chapter is principally a discussion of the general pattern of the subcortical pathways of the fissures, and an hypothesis is propounded with regard to the defect, and tuberculosis handle very fairly the controversial matter involved in a discussion as to the relative merits of environment and heredity in causing these conditions. There are many omissions in the book; for example, a whole section dealing with anomalies of metabolism should have been included. One looks in vain in the index for references to oxaluria, cystinuria, pentosuria, porphyria. If they are treated they are not indexed, and there seems no logical place where they might have been included. The chapter on defects of the skeletal system leaves the inquiring physician as much in the dark as he was before he read it—much of theory but little to aid the physicians who is trying to advise a patient with syndactyly, ectrodactyly, multiple exostoses, Morquio's disease, etc. The assumption is made that because monsters can be produced experimentally, environment, and not germinal defect, is the primary cause. The repeated occurrence of spina bifida, anencephaly, hydrocephalus, etc., in a family does not fit in well with the environment theory.

There is no section dealing with defects of the reproductive system, and no section dealing with the inheritance of blood groups. The latter is not "morbid inheritance", it is true, but the medico-legal importance of blood-grouping, and the universal presence in the population make such a section worthy of inclusion. Moreover, blood-groups should accompany every pedigree of defects. Eosinophilia and microcytosis should have been included. The chapter on tumours is most inadequate, completely ignoring the data accumulated on this subject, even apparently misunderstanding what is meant by the term "hereditary." A very useful chapter on the methods of analyzing genetical data concludes the work, and should prove helpful to those not afraid of mathematical formulae. The average physician will probably skip this section, however.

**Influence of Heredity on Disease.** L. S. Penrose, M.A., M.D. 80 pages. Price 5s. H. K. Lewis, London, 1934.

This volume won the Buckston Browne Prize for 1933. It is divided into four sections, dealing with the laws of inheritance, with the statistical methods of studying human inheritance, with the application of these methods to the problems of epilepsy, Mongolism and epiloia, and finally with a forecast of the future of human genetics and its relation to medicine and eugenics. To the average physician who knows little, but who wants to know more of the rôle of inheritance in disease, the book will be disappointing, because few of the questions which he wants answered are dealt with. The mathematical treatment has been so condensed that for the

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non-mathematically inclined the second and third sections, which comprise four-fifths of the book, are unintelligible. Nevertheless, it is a helpful book to the student of human inheritance who already knows what diseases are inherited, and who knows enough of mathematics to appreciate the method of derivation and use of the formulae.

When the reader sees a mathematical approach to the subject, however, he wishes for a correct mathematical treatment. Unfortunately, this does not seem to be available when the author deals with the matter of elimination of mental defect from the population through prevention of breeding. Most workers in approaching this controversial topic assume, as has Dr. Penrose, that the feeble-minded and normal persons mate at random, and, in his particular problem, that the mentally defective mate 198 times as often with the normal persons as with one of their own intelligence level. On this rather questionable assumption he draws the conclusion that the incidence of mental defect would be lowered only 9 per cent every thirty years. Allowing this assumption to be correct, the figure should be 17, not 9; and I doubt whether anyone would agree that mental defectives find normal mates 198 times as often as mates of their own type. Penrose admits that if defectives tended to mate with defective more frequently than with normal persons his figures of 9 per cent would be significantly increased, but feels that this tendency for like to mate with like is manifested to such a slight degree that it does not modify his argument. In Canada, I am sure that the mentally normal do not tend to seek their mates among mental defectives to the extent which this treatise would suggest. Mathematics is an excellent handmaiden when the initial premise is correct, but is most misleading when the initial premise is as wide of the truth as this one undoubtedly is.

**Chinese Medicine.** William R. Morse, M.D., LL.D., F.A.C.S., Dean of Medical School, West China Union University, Chengtu. *Clio Medica* Series, No. 11, 185 pages, illustrated. Price \$2.50. Paul B. Hoeber, New York, 1934.

This little volume of 168 pages is a recent addition to the admirable "*Clio Medica*" series of pocket manuals on the History of Medicine. The author, who is Dean of the West China Union University, has had opportunity to observe at close range the present status of Chinese medicine, and has given us a well-written account of its development from the early periods of Chinese culture. The shackled association of medical beliefs in China with the ancient naive philosophic system has hampered any progress and has prevented any advance during the past thousand years. Anatomy and physiology as a basis for medical knowledge do not exist. The author points out that if the form and function of the human body "do not conform to philosophical reasoning, then hypothetical organs and channels are assumed." There is an intriguing chapter on "The Pulse", in which Dr. Morse emphasizes the value placed on the almost ritualistic examination of the pulse by the Chinese physician in diagnosis. The Oriental materia medica, one learns, assumes astounding proportions. In the use of its constituents, the Chinese are less concerned with pharmacological principles than with an attempt to overcome the disharmony between vital spirits and forces in the diseased person. Chinese surgery has lagged even behind medicine, largely from a religious scrupulousness in mutilating the body.

The author has drawn an interesting picture of the theory and practice of medicine in an ancient civilization, linked up with religion and tradition. He suggests, however, that the Chinese desire for practical results is gradually overcoming the traditional reverence for the past. One would judge that in the author's experience the newer generation of Chinese are willing to accept occidental methods in the practice of medicine and surgery. The book is carefully written, well illustrated, and contains a useful bibliography.

**A Diabetic Manual for the Mutual Use of Doctor and Patient.** Elliott P. Joslin, M.D., Clinical Professor of Medicine, Harvard Medical School. Fifth edition, 224 pages, illustrated. Price \$2.00. Lea & Febiger, Philadelphia, 1934.

Joslin believes that the diabetic should know what his condition is, to what particular dangers he is exposed, what treatment is used, and what may be expected from treatment carried out under medical supervision by a cooperative patient. The book is almost perfect in its presentation of a fairly complex problem. It is an excellent example of how the printed word may be used to supplement the instructions given to individuals by their physician. "No diabetic should let three months go by without a visit to a physician" is the axiom laid down, and no patient, having read the book, would feel encouraged to consider himself capable of doing without his physician. It is evident that the author has drawn on his great experience, and that he has written this book with an appreciation of what patients need to know, where mistakes are made, and at what points encouragement should be given.

This book is recommended without reservation for the purpose for which it was written.

**Practical Methods in Biochemistry.** Frederiek C. Koch, M.S., Ph.D., Professor of Physiological Chemistry, University of Chicago. 282 pages, illustrated. Price \$2.25. William Wood & Co., Baltimore, 1934.

This excellent laboratory manual "is intended to present for medical students the more important qualitative and quantitative chemical aspects of cell constituents, of cell activities, and of the composition of blood, secretions, and excretions." The quantitative procedures given have been carefully selected, only the best amongst those of tested accuracy being included. While certain explanatory matter is inserted to assist correlation with theory, "no attempt has been made to interpret the significance of the results in blood and urine analysis." While the book therefore makes no pretence to be used for clinical purposes it can be thoroughly recommended in the specific field for which it is designed. The size, appearance, and price are highly commendable.

**Nature, M.D.** Richard Kovacs, M.D., Clinical Professor of Physical Therapy, Polyclinic Medical School and Hospital, New York. 181 pages. Price \$2.00. D. Appleton-Century Co., New York and London, 1934.

This book is a new addition to the Appleton Popular Health Series. In simple language the author explains what physical therapy is, how and when it is used, and what results may be expected from its proper use, as prescribed by a competent physician. He warns that "any physical measure that is powerful enough to do good is just as likely to cause harm if improperly applied." Of real value are the sections dealing with the limitations of physical therapy because of the absurd lengths to which such therapy is sometimes pushed. The book is recommended to anyone desiring to read a short but comprehensive account of the uses of heat, light, water, electricity, massage, exercise and rest as therapeutic agents.

#### BOOKS RECEIVED

**Essentials of Medical Electricity.** Elkin P. Cumberbatch, M.A., B.M., D.M.R.E., M.R.C.P., Medical Officer in Charge, Electrical Department, St. Bartholomew's Hospital. Seventh edition, 508 pages, illustrated. Price 10/6 net. Henry Kimpton, London, 1933.

**Essays on Chronic and Familial Syphilis.** Griffith Evans, M.A., D.M. (Oxon.), F.R.C.S., Hon. Surgeon, Caernarvonshire and Anglesey Infirmary. 91 pages. Price \$2.50. John Wright & Sons, Bristol; Macmillan Co., Toronto, 1934.